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THE COVER: The stylized beam reflecting from the man on the cover suggests this month's feature topic, the diagnostic uses of Ultrasound.

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1) All articles intended for publication should be submitted to the editors before the deadline which is usually six weeks before the release of the Journal.
2) Submitted articles should be typed (or legibly printed) double-spaced; single-sided on paper 8½" x 11" (letter size) and they should not be more than 15 to 20 pages (3000 to 4000 words)
3) Illustrations, graphs, diagrams, figures and photographs should be put on a separate sheet and identified by Arabic numerals. A list of explanatory legends for all the figures and diagrams should be put on another sheet. Do not write on the back of photographs.
4) References should be checked with the original sources, designated by Arabic numerals in the text, numbered in order of appearance and put on a separate sheet. Each periodical reference should include in order: the author's name and initials, title of the article, Journal name, volume number, page number and year. (e.g., 1. ROSEN HJ: Lumbar invertebral disc surgery: review of 300 cases. *Can. Med Assoc J., 101: 317, 1969.)*
5) The editors reserve the right to make such editorial changes as are deemed necessary to ensure correctness of grammar and spelling, clarification of statements and conformity to Journal style.
6) Acceptance for publication is subject to the understanding that such material is submitted solely to the Journal, and will not be reprinted without the consent of both the editors and author.

DIAGNOSTIC ULTRASOUND: A PRACTICAL REVIEW

by

Nick Rizos 7T8

Diagnostic Ultrasound has rapidly become a most versatile tool in the practice of medicine. The purpose of this review is to acquaint the medical student and physician with one type of ultrasound examination, the two-dimensional imaging method referred to as Compound B-mode display. In addition, the Real-Time instrument, capable of providing moving pictures, will also be discussed. However, all types of Diagnostic Ultrasound are summarized in Table 1.

There are basically three kinds of ultrasound equipment designed to give two-dimensional cross-sectional views: bi-stable (black and white), grey-scale (many different shades of grey), and real-time (moving pictures). Image quality has been improving at a rapid rate, paralleling technological advances. This has led to numerous clinical investigations into the feasibility of examination of a wide variety of anatomical sites and clinical conditions, and many of these are listed in Table 1. However, it must be understood that *there are relatively few established indications for routine ultrasound examination*. The common ones are marked in bold type in Table 1. The others *depend upon the particular interests and experience of the staff* of any particular Ultrasound service, *and upon the equipment* of that service. *One should inquire before making a referral.* There are about nine Ultrasound centres in Toronto, some of which have the more advanced grey-scale equipment. Real-time equipment is less readily available, as it is a recent development. Some centres limit their work, such as for obstetrical services only.

It will be obvious to the informed reader that some statements or terms appearing in the text are inaccurate. These have been allowed for the sake of easy comprehension of important concepts by the general reader.

TABLE I

A-MODE
Echoencephalography -midline shift
TM-MODE
Echocardiography
COMPOUND B-MODE
(Bi-Stable & Grey-Scale)
Obstetrics:
- Gestational Age
  - **Bi-Parietal dia.** -single or serial
  - Crown-Rump length
- **Placental Localization**
- **Trophoblastic Disease**
- **Multiple Gestation**
- **Oligo/Polyhydramnios**
- **Hydro/Anencephaly**
- Some Fetal Deformities
- Fetal Death Ascertainment

Gynaecology:
- **Neoplasm**
- Retained Products of Conception
- Other

Abdomen:
- **Liver** -size
  - -metastasis
  - -obstruction
- **Kidney** -size
  - -percutaneous aspiration
  - -radiation shield placement
  - -lymphcyst
- Pancreas -pseudocyst
  - -tumour
- Vasculature -**aortic aneurysm**
- Bladder -tumour
  - -residual urine
- Abscesses
- **Neoplasm**
- Gallbladder -size
  - -stones

Thyroid:
- **Cystic vs. Solid Masses**

Eye
Breast
Prostate
Testicle
Miscellaneous
REAL-TIME MODE
Obstetrics
Cardiology
DOPPLER MODE
Heart Valve Motion -fetal heart
Peripheral Blood Vessel Flow
-thrombosis

Theory

Some knowledge of basic principles will aid in understanding why ultrasound is helpful in the diagnosis of certain conditions but not in others. Furthermore, it will facilitate rapid orientation and interpretation when examining the ultrasound scan.

Information is obtained by ultrasound from the detection of reflections. The technique is non-invasive. It requires no contrast media. The reflections occur at interfaces between two anatomical structures of different density. The greater the difference in density, the greater the intensity of the reflected signal. If a signal is strongly reflected, there is weak penetration beyond that interface. Therefore, less information can be obtained about structures behind a strongly reflective interface. "Shadows" can therefore occur.

The vibrating source is placed in contact with the skin and the vibrations are transmitted through deeper structures. Ultrasound differs from audible sound in its frequency of vibration, the former being three orders of magnitude higher. There are certain properties which depend upon the frequency. At low frequencies, such as in the audible range, sound is omnidirectional: an electronic loudspeaker can be heard whether it is facing toward or away from the listener. This holds true particularly for sounds in the bass range, and less so in the treble range. At the higher frequencies of ultrasound, a narrower beam is achieved. Therefore, only structures in the body which are directly in the line of the beam will produce echoes. Secondly, a higher frequency permits greater resolution, but achieves less penetrance. Therefore, a regular low frequency element functions well for abdominal scanning, but gives poor resolution in ocular scanning, whereas an ophthalmic high fre-

quency element will yield poor visualization of abdominal organs due to poor penetration. It is therefore important to determine whether the local Ultrasound service has the required equipment for a given scan, since the apparatus is not universal in its application.

Let us return to the concept of the interface. The first interface encountered by the outgoing beam is the surface of the skin. If a small air gap is inadvertently allowed to intervene, due to imperfect skin contact of the source, a large reflection will occur, resulting in poor penetration. The large reflection is the result of the large difference in density between air and skin. This yields hopelessly weak reflections from structures within the body. To solve the problem, a *coupling agent* is used on the surface of the skin. A *layer of mineral oil* is applied to the region to be examined. This proves to be effective: the oil/skin interface is far less disruptive than an air/skin interface.

Similarly, if bone is encountered by the beam, one can expect a large reflection and poor penetration due to the large bone/soft tissue density difference. Therefore, a shadow, i.e., a region of no information, is seen behind bones. For example, the adult heart is not visualized through ribs, but must instead be viewed through a "window" of soft tissues, namely the intercostal space.

Another bothersome interface is that which is encountered in gas-containing viscera. This can be so severe as to make a scan totally useless. Generally speaking, the only real solution is to scan again at a later date. Gas in the GI tract usually does not interfere with routine scans of uterus, liver, and kidneys (when scanned through the patient's back), whereas other abdominal regions are often obscured by shadows created by the large soft tissue/gas interface at the wall of the gas-containing viscus.

The resolving ability of ultrasound units is improving as the state of the art improves. It depends, of course, on the surroundings of the lesion in question. A small cyst in a heterogeneous mass would be difficult to see, whereas a small solid tumour on the posterior wall of a full bladder would be easy to see. Resolution also depends upon the quality of the scan, which in turn depends upon the scanning technique and the calibration of the electronics.

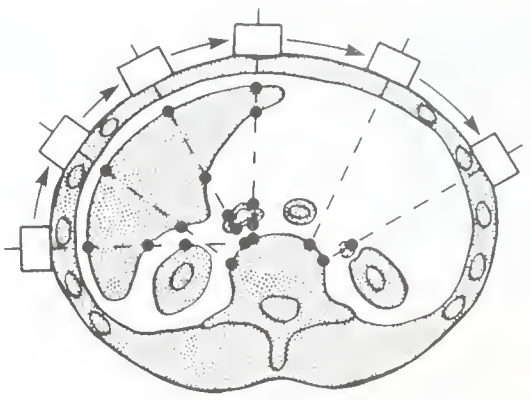


Fig. 1. Scanning technique for B-mode.

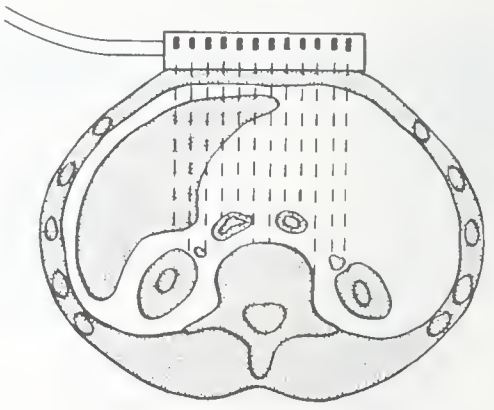


Fig. 2a. Linear array scanning in Real-Time unit.

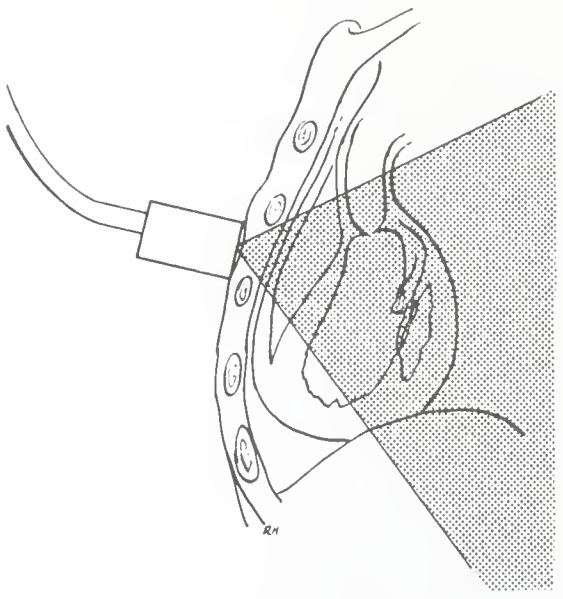


Fig. 2b. Real-Time sector scanning of heart through intercostal space

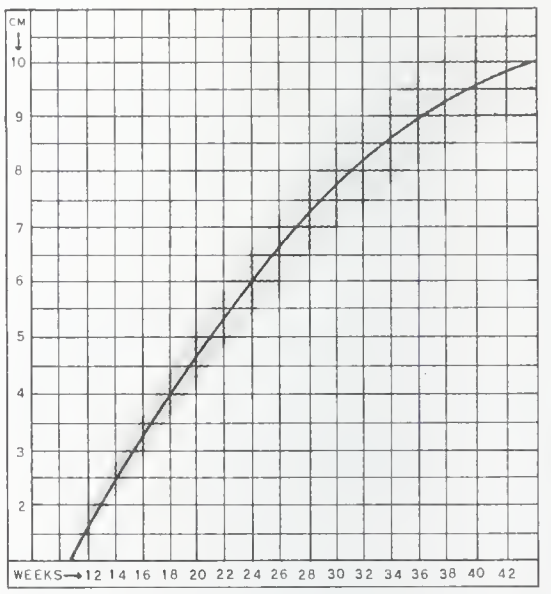
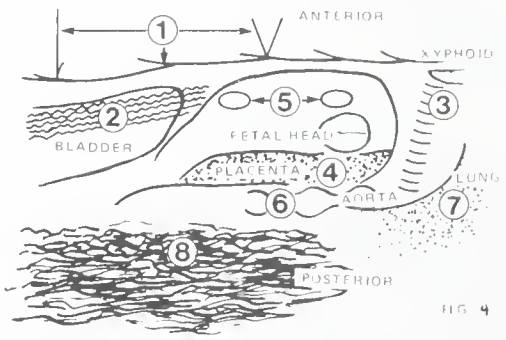


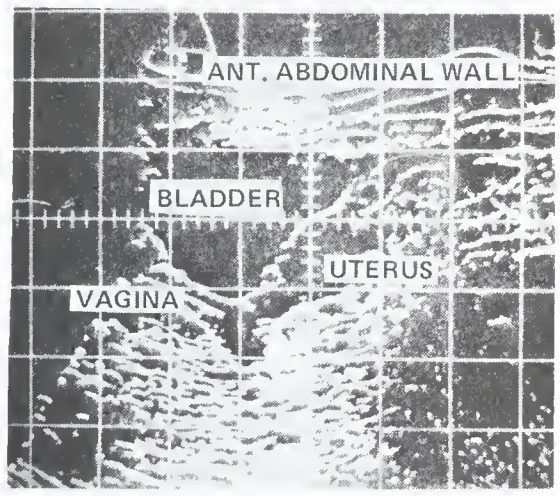
Fig. 3. Gestational Age vs. Biparietal Diameter

ARTIFACT IN ULTRASOUND



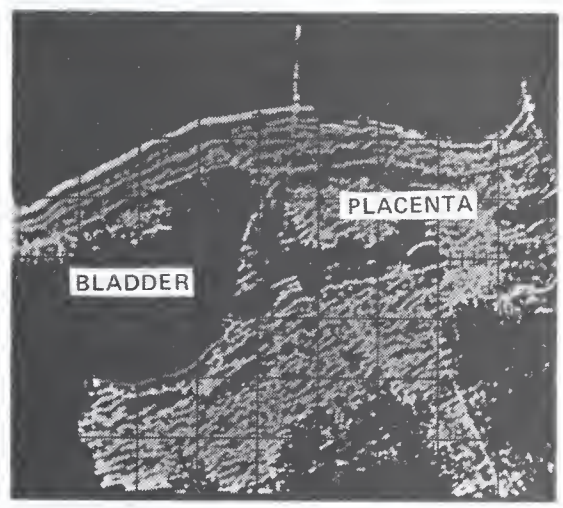
(1): Marks can easily be made to indicate the location of the umbilicus and symphysis pubis. The surface of the skin may appear jagged, but it merely traces the path of the probe sectored back and forth along the skin. (2): A strip of echoes is frequently seen within a cystic mass, such as the bladder, parallel to the near wall. (3): Reverberation from a powerfully reflective interface, such as bone/soft tissue, or gas/soft tissue, results when a single pulse of Ultrasound is repeatedly bounced back and forth between this powerfully reflective surface and the surface of the source/receiver.Each time the pulse returns to the receiver, it is interpreted as an echo from a progressively deeper structure. The elapsed times of the artifactual echoes are exact multiples of the original echo, so they are represented as parallel, equally spaced lines as the source/receiver is passed over a bone or gas-filled viscus. (4): Poor penetration of the beam through the fetal head (or other reflective mass) results in poor visualization of deeper structures, in this case a portion of the posterior wall placenta. Thus, a 'shadow' is produced. (5): A single, distinct structure, such as a fetal limb, may appear twice in the same Compound B-Mode scan picture if it happens to move quickly and is visualized in both locations in the course of slow manual sectoring over the abdomen with the probe, or by repeated sectoring and superimposition. This cannot occur with Real-Time imaging. (6): Pulsatile structures such as the aorta may appear wavy, since the probe's beam passing longitudinally over them will record the instantaneous diameter at each point. This cannot occur in Real-Time imaging. (7): In abdominal scanning, echoes are frequently seen deep to the diaphragm in sagittal sections not near the midline, in the lung field. This may be related to the concavity of the diaphragm and resultant mirror-imaging of subphrenic structures. (8): Meaningless echoes are seen in the deep regions.

The following are examples of Ultrasound scans of the three types of Compound B-mode: bi-stable (BS), grey-scale (GS), and real-time (RT). Some of the examples required a certain degree of extra effort and technical sophistication. Generally speaking, it is wise to determine the capabilities and limitations of the local Ultrasound service before referring a patient for examination.



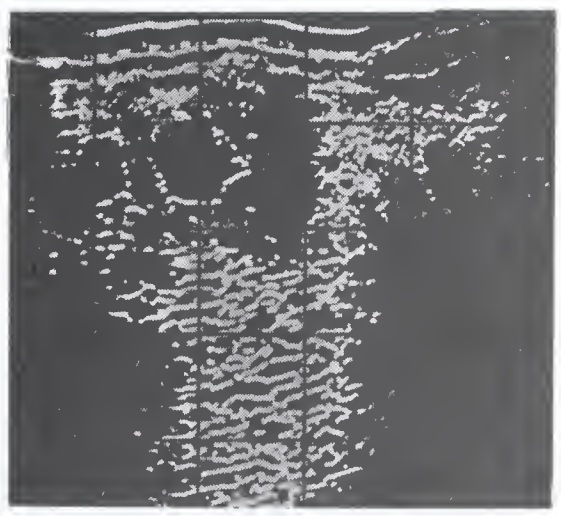
Case 1: Non-pregnant female (BS). Midline sagittal section

The full bladder gives good visualization of the vagina, posterior fornix, and uterus. Otherwise, the bowels would enter the pelvis and obscure these features.



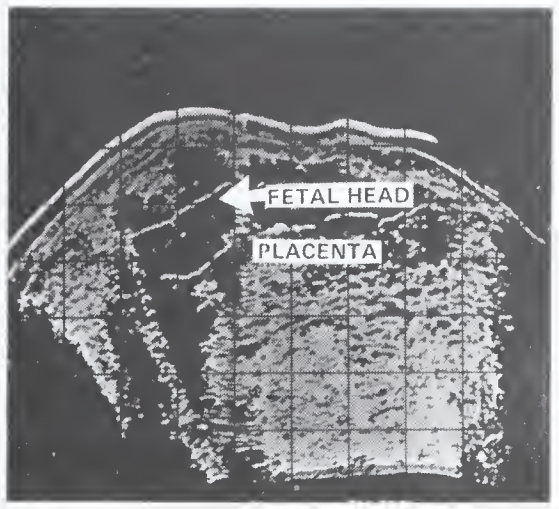
Case 2: Pregnant female (BS). Sagittal section

The placenta is visible within the uterine outline. This is not a midline section, and the amniotic space is not transected. The echoes within the bladder, along its anterior wall, are artifact. This artifact is characteristic of all anterior borders of cysts.



Case 3: Early gestation, 6.5 weeks (BS). Sagittal section

The gestation sac is visible, but no fetal parts or placenta can be discerned yet. The bladder was poorly filled for this examination.



Case 4: Pregnancy, 26 weeks, posterior wall placenta (BS). Transverse section

The fetal head can be seen, with a midline falx cerebri. This indicates that the bi-parietal diameter is being visualized. The intracranial echoes in the hemisphere closest to the surface of the maternal abdomen are artifact. The posterior wall placenta is well visualized. However, there is a shadow from the fetal head.

The Scanning Technique

The ultrasound cross-sectional image is produced in the following manner. One beam appears on the picture screen as one line composed of dots representing echo-producing interfaces. The dots are spaced according to the elapsed time between echoes. If an infinite number of such lines is plotted, all properly oriented relative to one another on the picture screen (this infinite number of lines is achieved by sweeping the transmitting and receiving element over the oiled surface of the skin), a two-dimensional picture is obtained (figure 1). Of course, this requires a mechanical arm to be attached to the source, having proprioceptive electronic components in its joints. This supplies the necessary information for the electronics to properly orient each line of dots on the screen. Thus, a plane is defined, and a true cross-sectional view of the body is obtained. This is the Compound B-mode scan. It is a still picture. It can be either a bi-stable display or a grey-scale display, depending upon the electronic sophistication. The grey-scale unit extracts and displays more information pertaining to the nature of the echoes, compared with the older bi-stable method which basically represents all echoes equally on the picture screen.

The real-time mode is simpler to operate. One type has a linear array of over sixty source/receivers built into a hand-held block (figure 2a). This block is placed on the oiled skin. The display consists of over sixty closely spaced parallel lines composed of white dots of variable intensity. The image changes many times a second, similar to the principle of television or fluoroscopy. The lightweight block can, when held still, visualize movement such as vessel pulsation or fetal movements, or can be rapidly repositioned under direct visual control to facilitate the search for findings of interest.

Another type of real-time device does not have a linear array of source/receivers, but instead has a source/receiver which rapidly and repeatedly scans an 80° sector from the tip of a small probe, producing many images a second. This is particularly suited to heart studies, where it may sector a view behind adjacent ribs by "looking" through an intercostal space (figure 2b). This unit is fundamentally different from the older and much less expensive Time-Motion echocardiography device, which plots one time axis and the other axis corresponding to distance from the probe. The real-time unit provides true cross-sectional motion picture views.

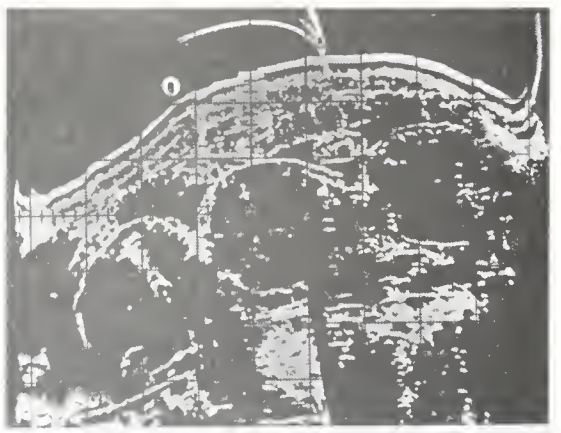
Obstetrics

The commonest use of ultrasound is probably for estimation of gestational age. The traditional method involves measurement of the fetal bi-parietal diameter. It has been found to correlate well with gestational age (figure 3). However, the 95% confidence limits are wider later in the pregnancy, so an earlier initial examination (such as between 16 and 20 weeks of estimated gestational age) is much preferred over a later initial examination. On the other hand, an examination much earlier will often fail to visualize the smaller fetal head. In the range of 7 to 12 weeks gestation, some centres, notably in Britain, estimate gestational age by measuring crown-rump length. However, this is not a common practice. It is important to determine the time of the pregnancy at which the local Ultrasound service prefers to perform initial scans.

With a reliable initial scan, serial scans for bi-parietal diameters can yield a graphical plot which can aid in the assessment of such conditions as intrauterine growth retardation. The Ultrasound service will recommend repeat appointments at optimal intervals of time.

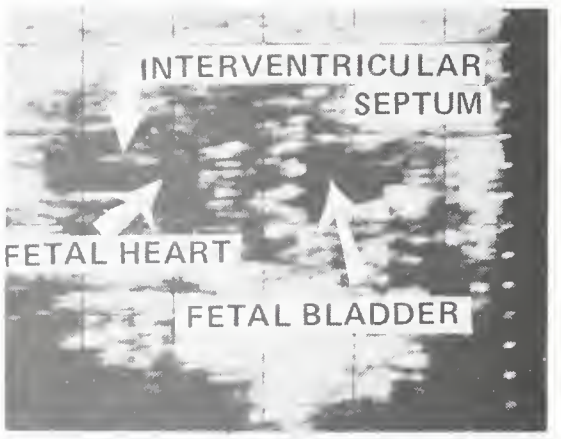
Placental localization is another common indication. The placenta is usually well visualized, for amniocentesis site determination, or assessment of suspected placenta praevia. One exception is the posterior wall placenta, which is often obscured by shadows from the fetus. A full bladder is essential, particularly when it is important to visualize the lower uterine segment. It permits the beam to travel anteroposteriorly from bladder to uterus, resulting in little density difference and therefore excellent penetration and visualization. In addition, the anatomy is better defined when the bladder is made to be a significant space-occupying viscus. Furthermore, the bowel is pushed superiorly and out of the way by the bladder in early pregnancy. It is not practical for the bladder to be filled after the patient presents for examination with an empty one. Giving water to drink in such a situation is rarely done, as it tends to create problems in appointment schedules.

Finally, it is important to understand that Ultrasound is not a form of ionizing radiation, as X-rays are. Therefore, *do not* tell an inquisitive obstetrical patient that "ultrasound is just like x-rays." It is wise to point this out to nursing and reception desk staff. This problem is a source of anxiety among patients who know that radiation is harmful to the fetus.



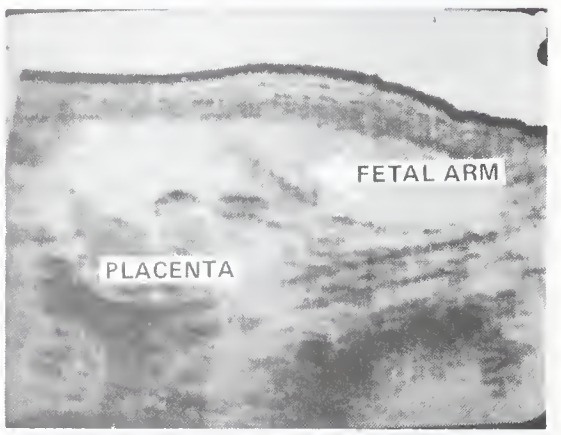
Case 5: Multiple pregnancy, 27 weeks (BS). Sagittal section

Although three circles are seen, this particular patient had twins and not triplets. The third circle is a section through a fetal trunk. This serves to emphasize the fact that more than one section is required before an interpretation can be made. An anterior wall placenta is also seen.



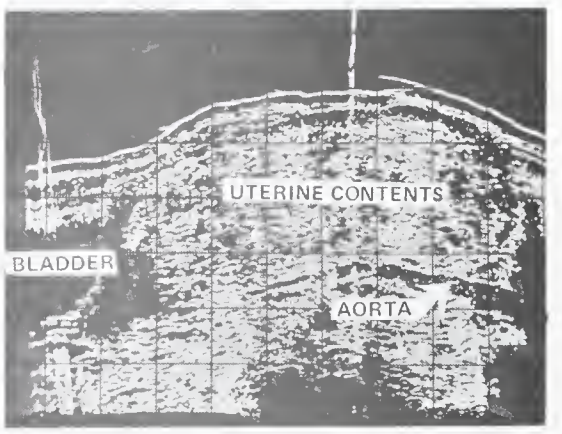
Case 6: Fetal trunk, showing fetal heart chambers and fetal bladder (RT). Sagittal section

With the real-time scanner, the heart beats were visualized in motion picture-like fashion, when this photograph was taken. Similarly, bladder emptying and fetal thoracic respiratory movements can be seen in a fetus after a certain age. Of course, gross movements of body and limbs are easily seen.



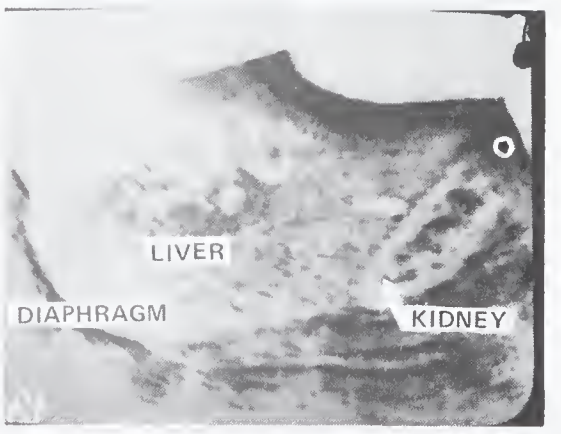
Case 7: Fetal limb, and posterior wall placenta (GS). Sagittal section

This section passes through a fetal limb, clearly showing part of the shoulder, the entire upper arm, elbow, forearm and hand. The shoulder and upper arm are lying against the posterior wall placenta.



Case 8: Trophoblastic disease, 18 weeks (BS). Midline sagittal section

A suspicion of this disease is one of the indications for ultrasound examination. This is an obvious advanced case. However, nothing can be said about the histological nature of the disease. The grape-like vesicles provide the multitude of echoes, in a characteristic "snowstorm" pattern.

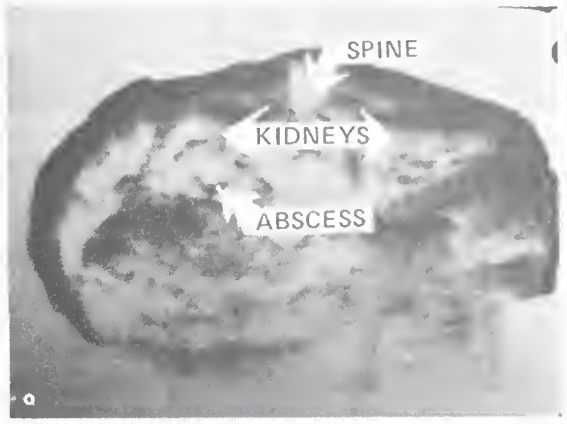


Case 9: Liver (with metastases), and right kidney (GS). Sagittal section

The liver is clearly enlarged, with areas of metastases from a pelvic primary.

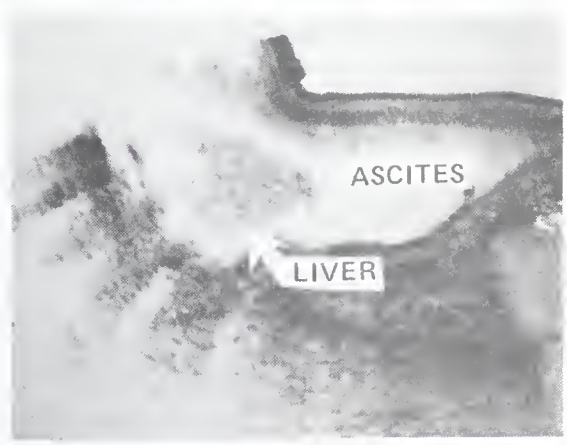
Case 10: Acute pyelonephritis, left kidney (GS). (a) transverse section, (b) sagittal section

This scan was obtained after an IVP and retrograde pyelogram failed to visualize the kidney with its abscess. The normal right kidney shows the pelvicalyceal system in normal configuration. (However, the right kidney is partially obstructed in this section by reverberation artifact generated by the twelfth rib. This results from repeated back and forth reflections between the bone and sound source, with multiply-detected echoes, once for each time the source/detector is encountered.) The left kidney shows cystic dilatation of the renal pelvis. The sagittal section served to localize the abscess and a percutaneous aspiration of 50 ml of pus was then performed at a depth of 5 cm.



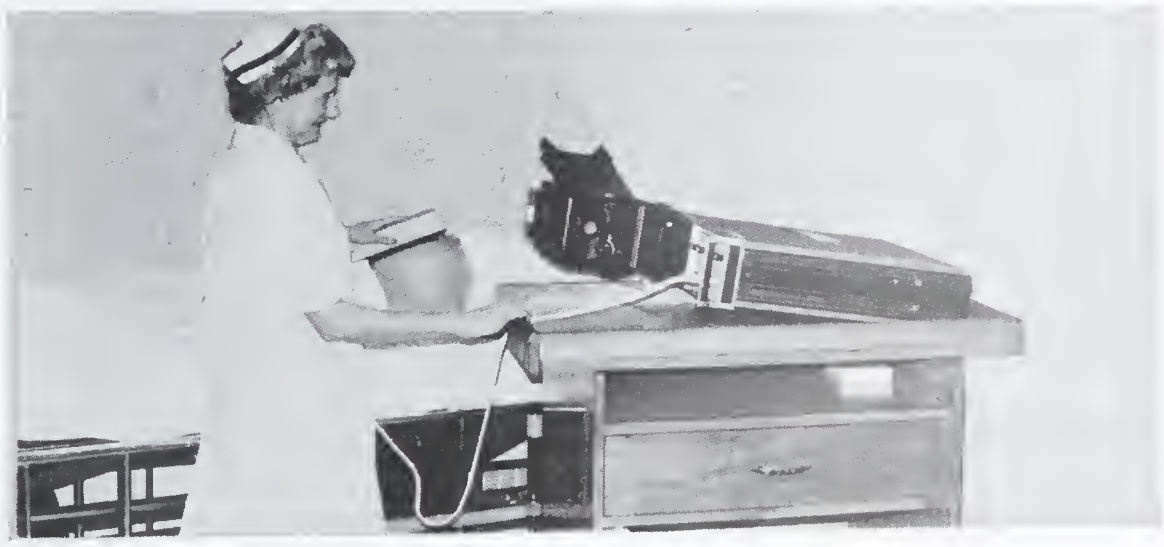
Case 11: Liver, with peri-hepatic and flank ascites (GS). Sagittal section, 10 cm right of midline

In this section, the liver is clearly shown, with its inferior edge hanging limply in ascites fluid in this supine patient. The ascites was the result of pelvic carcinoma.



Case 12: Abdominal aorta, showing coeliac axis (GS). Midline sagittal section

The coeliac axis and two of its branches can be seen arising from the aorta. The overlying liver is also seen. No contrast medium was required.



At left is shown the Real-Time linear array scanning device while being used for an Obstetrical examination. It is a portable unit, and is seen here situated on a table. The hand-held block is shown positioned for a midline sagittal view. A Polaroid camera can be seen attached by a hinge to the front of the tabletop unit, where there is located a black-and-white picture screen. Photographs can be taken after swinging the camera into position in front of the screen.

Because of its non-ionizing nature, Ultrasound has met with wide acceptance in Obstetrics. Nevertheless, some experts have argued that twenty years of obstetrical experience with ultrasound may not be adequate for the appraisal of long term deleterious effects on human tissues.

Abdomen

It is essential to determine, before an appointment is made, whether the local Ultrasound service is capable of or willing to examine specific abdominal structures. This is highly dependent upon the experience of the staff, liason with specialty departments, and the equipment available. For example, neoplastic masses can be routinely assessed in some centres specializing in cancer, but probably in few other centres.

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ECHOCARDIOGRAPHY

by Peter Liu 7T8

Brian Gilbert M.D., FRCP(C)

Introduction

Echocardiography is the new "wonder child" in the field of non-invasive cardiology. Still in its adolescence undergoing further development and maturation, it has already demonstrated tremendous potential in providing valuable diagnostic information with absolutely no risk to the patient. The echocardiogram itself, however, often looks bewildering to the untrained eye, for it bears no resemblance whatsoever to the physical structures under study. It is the purpose of this article to acquaint the general reader with the basic interpretation and application of the echocardiographic image. The effort is by no means exhaustive, and is only intended as an introduction.

The Principle

Echocardiograms are obtained by placing on the patient's chest a transducer containing a piezoelectric element, which will produce a brief pulse of ultrasound upon electrical stimulation. Each pulse usually lasts one microsecond, and the frequency most commonly used is 2.25 Million Hz in order to optimize both penetration and resolution. Just as light passing from air to water gives off a partially reflected ray, as the ultrasound beam passes through the tissue, echoes are reflected from interfaces between materials made of different acoustic impedance (e.g. between myocardium and blood.) The greater the difference in impedance, the louder the echoes reflected. The transducer also acts as a receiver and "listens" to the echoes for the next 999 microseconds after transmission, and then converts the sound energy into electrical impulses which can be displayed on the oscilloscope. The elapsed time between transmission and reception of the echo is interpreted by the machine and converted into relative units of distance.

There are three ways in which this information can be displayed (fig. 1):

The "A" Mode or Amplitude Modulation, in which each echo is represented by a vertical line and the height (amplitude) of each line represents the "loudness" of the echo. The lines shift back and forth as the structure under examination moves towards and away from the transducer.

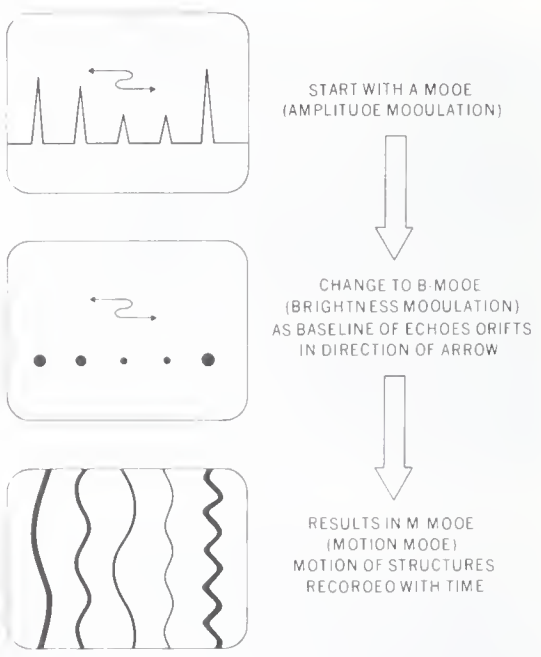


Figure 1. The three modes of displaying the echo information. The "M" mode with motion vs. time is the display of choice in modern echocardiography.

The "B" Mode or Brightness Modulation, in which the A Mode display is turned on end, each vertical line thus becomes a dot, and the brightness of each dot represents the amplitude of the echo.

The "M" Mode or Motion Mode, in which the Brightness Mode is displayed across the screen against time. As the structures oscillate back and forth, the dots representing them do the same and trace out a pattern of motion versus time. As the heart is a dynamic organ, the "M" mode is the display of choice in almost all cases.

A permanent record of the display can be obtained by photographing the oscilloscope with Polaroid film, or more commonly by means of a direct tracing onto light sensitive paper.

The Technique

Operation of the complex echocardiographic equipment requires the expertise of a physician or a specially trained technician. The patient is examined in the supine or left lateral position with the transducer positioned lateral to the left sternal border in one of the interspaces between the second and sixth rib. "Acoustic windows" represent bone- and lung-free areas through which the ultrasound is able to pass without much interference. They may be very large as in children with unossified sternum, or very small in a patient with emphysema or chest wall deformities. The ultra sound beam should be directed vertically towards the structure under examination. With proper angulation and fine adjustment of the sensitivity and damping factors, quality echocardiograms can be achieved with regular success, especially as experience accumulates.

Motion of the mitral valve is usually the most readily recognized pattern on the echo tracing, and can be readily located. With the mitral valve as a landmark, the transducer can then be directed inferiorly and laterally to scan the details of the minor axis of the left ventricle. By retilting the transducer more superiorly and medially, the tracings of the left heart structures will be displayed in sequence, ending with the aortic root and the aortic valve (fig. 2). With skillful manipulation, the tricuspid and pulmonic valves are also within reach of the ultrasound beam and can be studied in some detail.

Current Application

Normal Mitral Valve

The most well established application of echocardiography is in the assessment of valvular disease, especially that of the mitral valve. Normal mitral valve motion is the key pattern to be recognized on the echo tracing (fig. 3). The normal anterior mitral leaflet inscribes an "M" shaped curve for each cardiac cycle, while the posterior leaflet mirrors a "W" shaped pattern, both reflecting the physiological events involved in the workings of the mitral valve. During systole (Points C-D), the closed valve within the mitral ring gradually moves towards the transducer

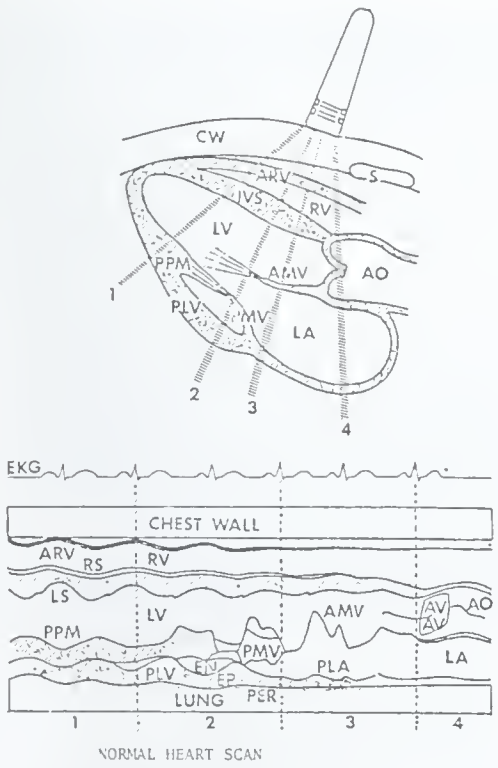


Figure 2. Structures of the heart scanned from position 1 to position 4. RV, LV = right & left ventricles; IVS = interventr septum; PMV, AMV = post. & ant. mitral leaflets, PPM = post. papillary muscle; AO = aortic root.

as the heart moves forward during ventricular systole. As valves open in diastole, the anterior leaflet rapidly moves towards the transducer (point E), while the posterior leaflet recedes from it. Thus the maximum opening of the mitral valve occurs almost immediately and simultaneously after the onset of diastole. By middiastole, the ventricular filling slows to a minimum and the mitral leaflets drift almost to a semiclosure (F). The rate at which the ventricle fills can be measured by the E-F slope, termed Diastolic Closure Rate, whose significance will come up again later. With atrial systole, the valves are sharply pushed open again (A), and this may be clinically associated with a fourth heart sound.

Mitral Stenosis

Rheumatic mitral stenosis is easily diagnosed on the echocardiogram. Due to the reduced valve area and thus delayed ventricular filling, the Diastolic Closure Rate (E-F slope) is markedly diminished from a normal value of 100 mm/sec to below 40mm/sec. The posterior leaflet moves in the same direction as the anterior leaflet apparently due to the commissural fibrosis and fusion. There is also reduced valve motion during atrial contraction (A). The pliability of the valve may be evaluated by the maximum extent of anterior leaflet excursion (D-E); calcification and fibrosis are reflected by multiple intense echoes. This information is important for the pre-operative evaluation of the patient with mitral stenosis. An uncalcified valve is amenable to commissurotomy, while a calcified stiff valve may necessitate a valve replacement. Selection of prosthesis can also be based on the echo profile of the left ventricular cavity. Post-operative evaluation of the success of the surgery can be safely and non-invasively carried out in some patients with serial echocardiograms.

Mitral incompetence is not readily detected on the echocardiogram, but its severity may be inferred from a large but well contracting ventricle and a large atrium, without signs of significant mitral stenosis.

Atrial Masses

Ultrasound is the best non-invasive method available for detection of left atrial masses, most of which are myxomas. They typically are represented by a set of dense echoes behind the anterior mitral leaflet during diastole.

Mitral Valve Prolapse or Mid-Systolic, Late-Systolic Murmur Syndrome

Echocardiography is invaluable in diagnosing this interesting and relatively common condition in which there may be myxomatous degeneration of the posterior and anterior mitral valve leaflets, with redundancy of the valve and chordae tendineae. Thus the leaflets sag back into the left atrium during systole. On echocardiogram, the normal anterior movement of the closed leaflets in systole (C-D) is replaced by either a sudden posterior motion (Midsystolic Buckling) of the leaflet away from the transducer (often coinciding with the click, due to the sudden ballooning of the valve back into the left atrium, fig. 4) or a gradual pansystolic bowing of the C-D slope.

Muscular Subaortic Stenosis (MSS) or Idiopathic Hypertrophic Subaortic Stenosis (IHSS)

The echocardiographic evidence can be used to rule in or rule out the presence of MSS (fig. 5). Classically, there is tremendous hypertrophy of the interventricular septum, with the ratio of septum to posterior wall thickness greater than 1.3. There is also a peculiar systolic anterior motion (SAM) of the mitral valve, which is the abrupt movement of the anterior leaflet to-

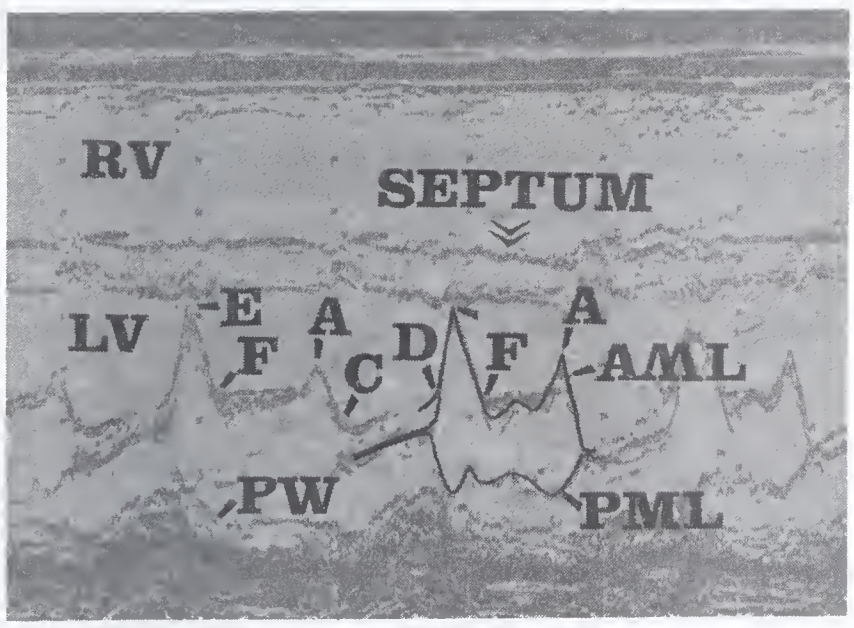


Figure 3. Normal mitral valve motion. Valves close in systole (C-D). Leaflets open maximally in diastole (E), then drift together to a semiclosure (F), finally open again in atrial systole (A). AML, PML = ant. & post. mitral leaflets.

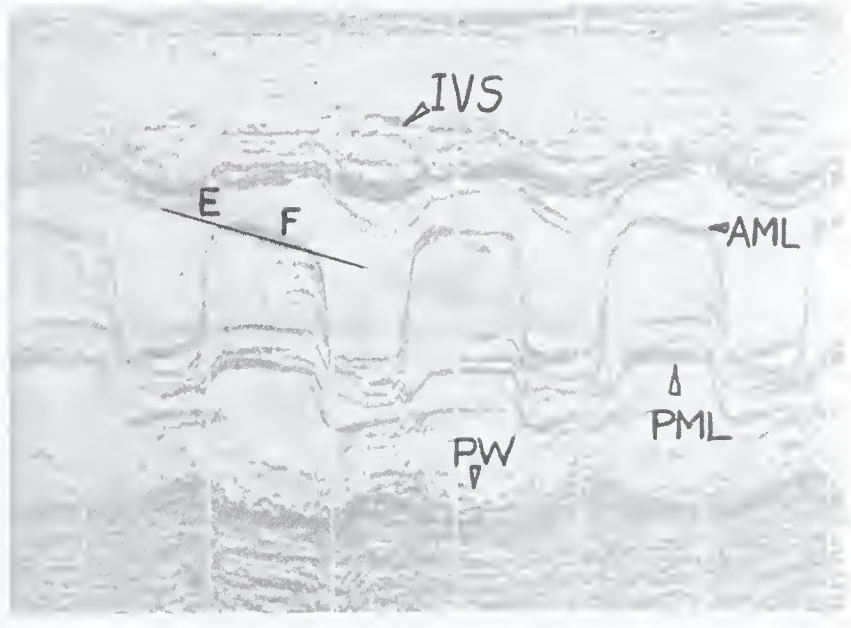


Figure 3B. Mitral Stenosis. Valve cusps are thickened, the post. leaflet (PML) moves anteriorly in diastole. The E-F slope is flattened with loss of "M" shaped motion of ant. leaflet (AML). PW = post. wall; IVS = interventr. septum.

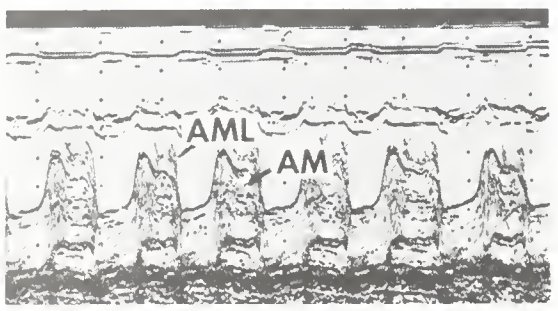


Figure 3C. Left Atrial Myxoma (AM). The ant. leaflet appears stenotic with dense echoes behind the valve in diastolic opening. AML = ant. mitral leaflet.

wards the septum drawn in by the rapidly ejecting blood through a narrowed outflow tract (thought to be due to a Venturi effect.) The stiffness of the hypertrophic ventricle with impaired filling contributes to the reduction of the E-F slope seen in these patients.

Aortic Insufficiency (AI)

The diagnosis of AI is established by noting diastolic fluttering of the left side of the septum and/or the anterior leaflet of the mitral valve, caused by the regurgitant jet. This is not correlated with the Austin-Flint murmur which is caused by turbulent antegrade atrioventricular flow through a progressively closing mitral valve in late diastole. In acute aortic regurgitation, one may see the classic early diastolic closure of the mitral valve as the ventricle is rapidly filled from the regurgitant blood. In the aortic valve itself, diastolic high frequency vibration of cusps may also be a sign of AI, but is not diagnostic.

Aortic Valve

The aortic valve is found between the echoes of the aortic root, which produce a pattern much like a "wavy road". During diastole, the valve leaflets approximate and form a single moving line in the middle between the two aortic root echoes. At the onset of systole, the valves open sharply with the right coronary cusp moving anteriorly and the non-coronary cusp moving posteriorly. Thus a "box" is formed between the "wavy road" during systole (fig. 6).

In **severe aortic stenosis**, the aortic cusps at times cannot be readily visualized. Presence of calcification gives the aortic root a layered appearance. **Mild** stenosis typically presents with thickened cusps with diminished opening and closing motion. Eccentrical position of closure of the cusps in diastole and asymmetry of leaflet images is suggestive of a **congenital bicuspid valve**.

In **supravalvular stenosis**, the supravalvular aortic area is narrowed but valve cusp motion itself remains normal.

In patients with **bacterial endocarditis**, diffuse thickening of the aortic valve image with normal cusp motion may suggest the presence of an infective vegetation on the valve leaflet. The vegetation may even be seen prolapsing into the left ventricular outflow tract in front of the mitral valve in diastole. The vegetations may show a high frequency rapid vibrating motion during the cardiac cycle.

Tricuspid Valve

The tricuspid valve resembles the mitral valve motion pattern, but usually only one cusp is seen by the echocardiogram at a time. **Tricuspid stenosis** also resembles mitral stenosis and is usually associated with mitral stenosis (with decreased diastolic closure rate and thickened valves). Tricuspid valve prolapse, fluttering of the valve with pulmonic regurgitation and Sinus of Valsalva aneurysms, and right atrial myxomas are analogous to their left sided counterparts.

Pulmonic Valve

Usually only one pulmonic valve cusp is visualized due to problems in angulation of the beam. The pulmonic valve has been useful in the analysis of **congenital heart diseases**, such as pulmonic stenosis. **Pulmonary hypertension** also has characteristic echo findings, but the details are beyond the scope of this article.

Pericardial Effusion

Clinical diagnosis of pericardial effusion can sometimes be very difficult, but the echocardiogram is capable of detecting an effusion of less than 100 ml with accuracy, and may detect an effusion as low as 20 ml of fluid. The accumulation of fluid in the pericardial cavity produces an echo-free space posterior to the left ventricular wall. The fluid space does not pass above the left atrium, thus differentiating it from a pleural effusion. Technically this can be a difficult examination to perform, and

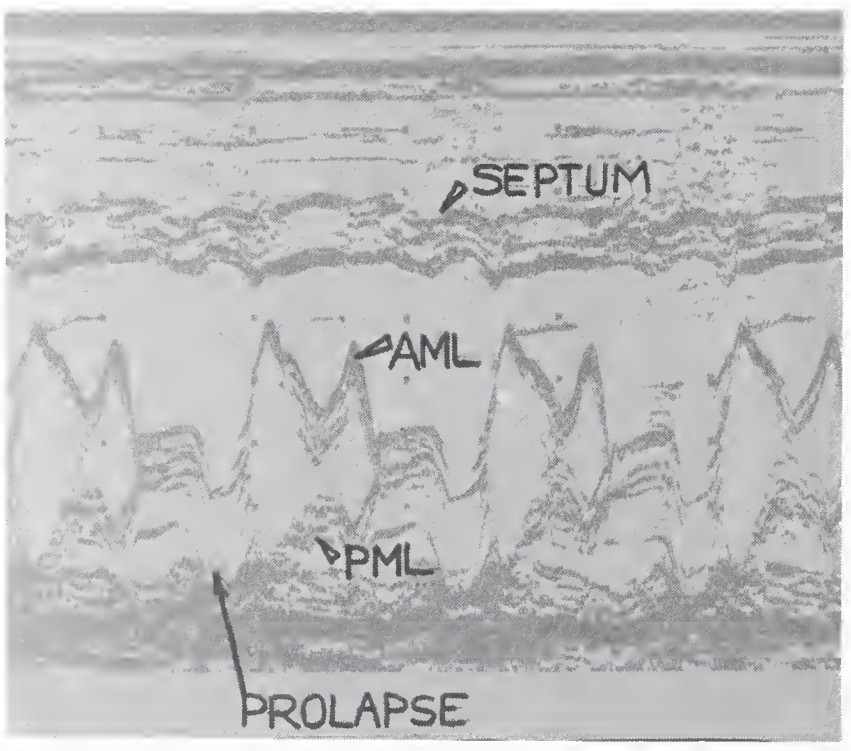


Figure 4. Mitral Valve Prolapse. The systolic closure line (C-D) moves back during systole (PROLAPSE). The post. leaflet (PML) sags back into left atrium. AML = ant. mitral leaflet.

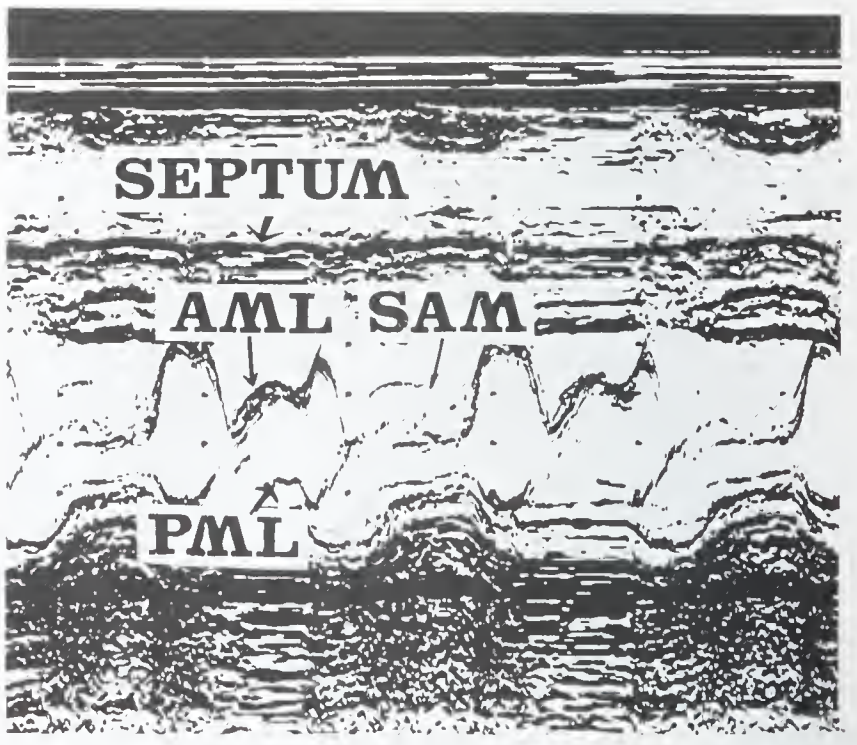


Figure 5. Muscular Subaortic Stenosis (IHSS) presents with thick poorly contracting interv. septum with reduced E-F slope and systolic ant. motion (SAM) of the ant. mitral leaflet (AML).

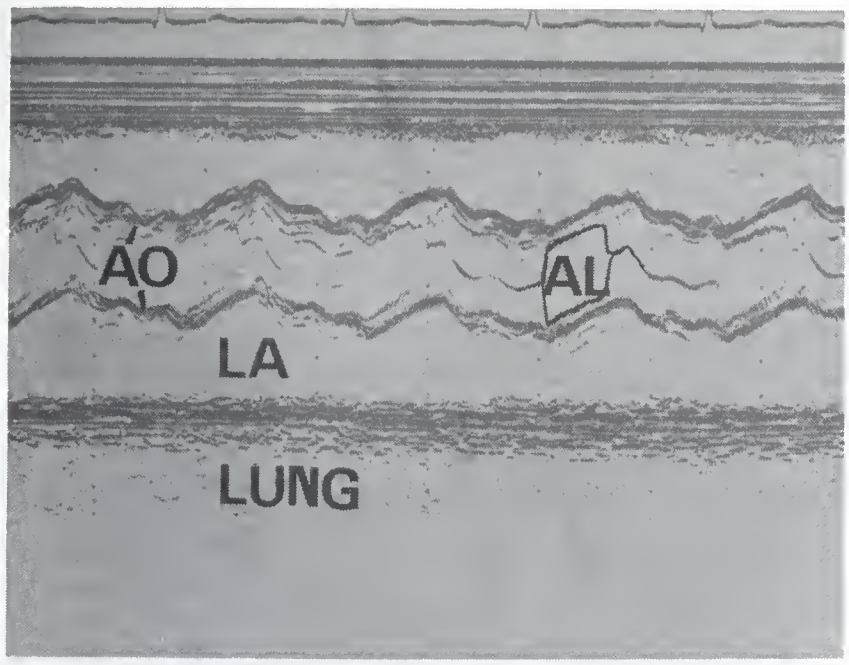


Figure 6. Normal Aortic Root with Aortic Valve. The symmetrical motion of the aortic leaflets (AL) during systole forms a "box" inside the walls of the aortic root (AO). Leaflets coapt in diastole.

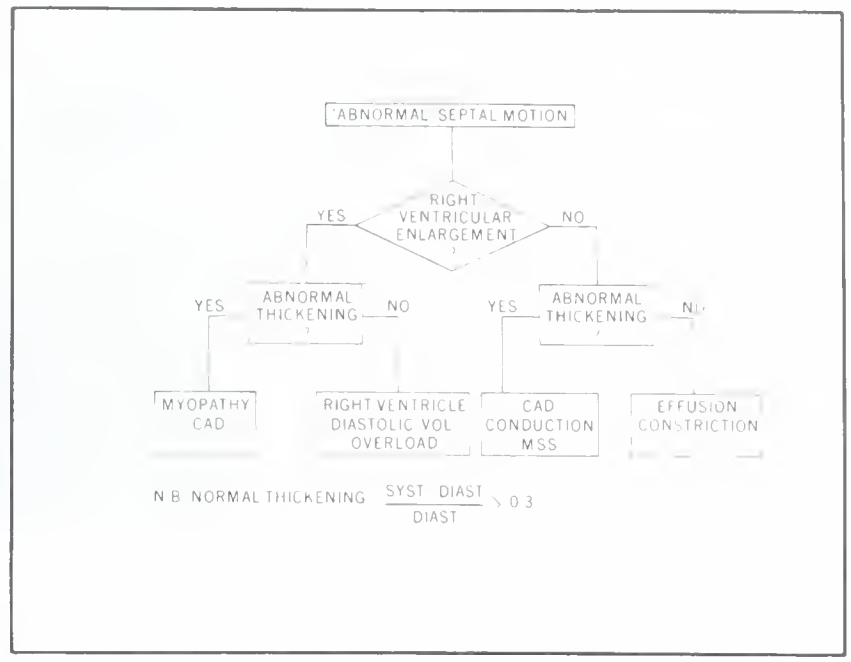


Figure 7. Approach to the differential diagnosis of abnormalities of the septum. (See text for details) CAD = coronary artery disease; RV = right ventricle.

there are many diagnostic pitfalls. The estimated amount of fluid based on echo data can be used to serially assess the progress of the patient.

Interventricular Septal Motion

Abnormalities in the interventricular septal motions *per se* do not constitute a disease entity, but it is of great importance in the differential diagnosis of other cardiac diseases associated with abnormal septal motion. The normal posterior motion of the interventricular septum during systole is best interpreted caudal to the mitral valve at the ventricular level. The septum, in addition to movement, also thickens more than 30% in systole than in diastole. Abnormalities of septal motion and abnormalities of thickening may both occur, either alone or in combination. A schema of differential diagnosis regarding abnormalities of the septum is outlined in fig. 7.

Lack of normal posterior septal motion has been described in conditions causing right ventricular diastolic volume overload, such as tricuspid insufficiency, pulmonic insufficiency and atrial septal defect. A large atrial septal defect is associated with "paradoxical" motion of the septum. In these conditions, the right ventricle is dilated but the septum thickens normally with each cycle of contraction. Similar lack of septal motion and right ventricular enlargement, but also combined with abnormal lack of systolic increase in thickness may be seen in patients with cardiomyopathy and coronary artery disease involving the left anterior descending vessel.

In MSS, both the septal motion and systolic thickening are minimal, but the massive thickness of the septum gives the diagnosis away. Classical left bundle branch block is associated with a sharp posterior septal motion shortly after the onset of the QRS complex. A similar abnormality has also been reported in patients with Wolff-Parkinson-White syndrome. Abnormal septal motion alone is seen in pericardial effusion, pericardial thickening and constrictive pericarditis.

Left Ventricular Function

Left ventricular measurements such as end-diastolic volume and end-systolic volume can be estimated by echocardiogram to assess the integrity of the myocardium. The ultrasound beam is aimed across the minor axis of the ventricle, just below the mitral valve and above the papillary muscle. During systole, from this vantage point the septum moves down toward the ventricle, while the posterior wall comes forward. Assuming a spheroid ventricular cavity, cubing the minor axis diameter at end-systole and end- diastole gives an approximation of the respective volumes (ESV and EDV). The stroke volume (SV) can thus be estimated: SV = EDV - ESV; as well as the ejection fraction (EF): EF = SV / EDV. These approximations become invalid if the ventricle is grossly dilated or extremely small as in children. In these cases, one may have to resort to complex formulae for correction.

Myocardial contractility can also be estimated by the mean velocity of circumferential fibre shortening, which is in turn calculated by the mean rate of change of the ventricular diameter with time. The higher the rate of shortening of the diameter, the better the contractility.

Right ventricular measurements are of limited value. However, gross dilatation can be readily recognized on the echocardiogram.

The Future

As experience accumulates and technique improves, new developments in echocardiography constantly bring the field towards maturity. The scope and limitations of the realm of echocardiography are just being delineated as the diagnostic precision is refined. New display techniques using multiple transducer arrays, phased array systems and mechanical sector scanner are now being studied to provide a two-dimensional image of the heart in the various phases of the cardiac cycle. The future that lies ahead is extremely bright because the echocardiogram provides such a wealth of information in a totally non-invasive manner.

An Interview with Dr. C. H. Best

by

Joseph Chu 7T8

Alan Ing 7T8

Nick Rizos 7T8

Journal: Dr. Best, can you tell us about your early work on insulin in Toronto in the '20's?

Best: Professor Macleod was the head of the department, and he was an authority, but he had failed to isolate insulin. He was away all that summer (1921) in Aberdeen, Scotland, so we didn't see anything of him at all, but when he came back, he took an interest, of course. We (Banting and Best) began working on the 17th of May, and by the end of August, we had completed many successful experiments in diabetic dogs, and I think 70 times we showed the substance (insulin) was there. Then, in November, we gave a paper for the faculty and research students at the medical school in Toronto. In December we went down to the States, to Yale, and gave a paper before the American Physiological Society. We then made a good lot of extract in early January, gave ourselves a big dose, and that was the beginning of clinical experiments at the Toronto General Hospital. Leonard Thompson was the first diabetic to get insulin. The clinicians at the hospital were overjoyed, of course. We had a friend, Dr. Joseph Gilchrist, who was a diabetic, and we worked on him in the laboratory.

Journal: What were some of the difficulties of insulin in early use?

Best: Insulin was not crystallized until 1926-27, and then we had a solution which was quite good. The chemical forms were, firstly, crystallization, which was done at Johns Hopkins University, and then by Scott in our laboratory, and then came the production of the slow-acting insulins, like Protamine Zinc insulin, which was made here by Scott and Fisher. It has now been synthesized, but that's not feasible on a large scale yet.

Journal: What was your relationship with Sir Henry Dale?

Best: I spent four years in Biochemistry and Physiology, and then in 1922, I got my M.A. in Physiology. The British government sent Sir Henry Dale over to see what was going on, and I made arrangements so that as soon as I got my medical degree, I'd go and work with him. That was in the summer of 1925. I worked there for two years with him.

He was a great authority on histamine, and when I was there, I discovered an enzyme which destroyed histamine, namely histaminase. We were the first to isolate histamine from normal tissues. So that was partly work that I was interested in before, and partly work that he had been interested in. I gave four or five papers at the Royal Society in London.

Journal: You have also worked with heparin, have you not?

Best: Yes, we purified heparin and used it for the first time, clinically, here. We proved in animals that it prevented thrombosis, and then Dr. Gordon Murray took it to the clinic, and that turned out to be a good show, I think. We then worked with a lot of other people on a substance that prevented degeneration of the liver. That turned out to be the simple chemical, choline.

Journal: Have you ever been enticed to leave Canada permanently to work elsewhere?

Best: In 1922, the Rockefeller Institute offered Dr. Banting and me stipends very much higher than we ever got in Canada, but we didn't go. We thought we had a responsibility here. I had been offered two or three jobs in London, and a Chair at Cambridge, and one at Edinburgh, and if my wife had wanted to go, I think we would have.

Journal: How would you compare the research centers of various countries, say the U.K., the United States, with those in Canada?

Best: Well, they've done an amazing lot in the United Kingdom: the crystallization and the physico-chemical structure. Of course, the greatest amount of research is in the United States. They've got more money and more people. In the States, they have a lot of influential people, many of them diabetic, to go up to the Congress, and they've obtained a lot of money. That hasn't been done in Canada, and the money that is available here is really very, very much too small. In England, the diabetics seem to contribute more, and they've been very successful as a result. The Scandinavian countries are very active, of course, too.

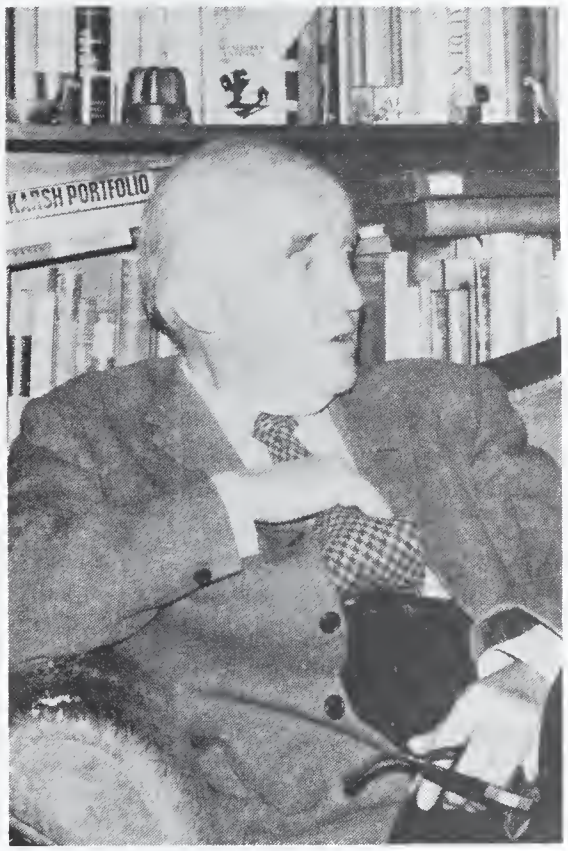
Journal: Speaking of the financial situation, there is currently a campaign on to raise money for the Canadian Diabetes Association, with a target of one million dollars. Can you tell us something about it?

Best: The problem is that more money is needed for research on diabetes in Canada. It is the Ontario branch of the Canadian Diabetes Association which is hoping to raise the money. They are having a lottery, and so forth. The idea of our (my wife and I) being out there at the Ontario Science Center was to try to help them.

Journal: That's where they have recreated the lab in which Dr. Banting and you did your work on insulin?

Best: Yes. It was put together about six or seven years ago.

Journal: Is the money to be raised going to be used strictly for research, or for other purposes as well, such as patient education?



Best: Well, research first, and then patient education. It is to be spent not only locally, but throughout the country.

Journal: How do you foresee the management of future research in Canada, in light of the current restraint on budgets?

Best: Well, the idea of this current campaign is not only to stimulate the government, but also to try to stimulate private sources. That's dropped off. There *must* be a lot of wealthy diabetics in Canada!

Journal: What sort of directions has research taken?

Best: Well, there's a great scarcity of insulin, and there's just a possibility of adapting some organisms, such as bacteria, to make insulin. Dr. Cecil Yip is doing work in Toronto in that direction.

Journal: Can you tell us about current work on the artificial pancreas?

Best: A lot has been done with respect to dogs and human beings, but the artificial pancreas is a room full of apparatus which needs to be miniaturized. They need money. And then, this business of transplanting Islet cells . . . it's been a failure up until the present, but it might easily be successful.

Journal: What are the current sources of pancreas?

Best: Beef and pig pancreas. There has also been use of sheep pancreas. Some people used fish pancreas, where the Islets are separate, you know, from the rest of the pancreas. That's a good source, but there's not much of it.

Journal: Can we next discuss your involvement with the Connaught Laboratories?

Best: I was the Director of the Insulin Division for many years. The University got 36 million dollars when they sold it, and the money should have all gone back into medical research, a lot of it. A little bit has, but not nearly enough, in my opinion.

The Connaught Laboratories work on all sorts of vaccines and antitoxins; insulin is still one of their big products. They have a monopoly on the sale of insulin in Canada. I think that should be maintained. I've seen in the papers that some people think it shouldn't be, but if they pull up their socks. . . . You know, it's awfully difficult to get enough pancreas now, so eventually, the insulin *will* be made synthetically, I guess.

Journal: In your opinion, what is it that draws a person into medical research?

Best: Well, I suppose they're motivated by the hope that they'll do something important!

Journal: And what of the difference between Basic Sciences Research and Clinical Research?

Best: Well, the Clinical Research people are very well trained in Canada and the United States. They have to have a lot of Biochemistry, Physical Chemistry, and Physiology, and they are able to do almost any type of fundamental as well as clinical research. They'd have a lot better income, and would get the satisfaction of doing both kinds of research, as a result of this training.

Journal: Can you tell us your opinion on what makes a *good* medical education?

Best: Well, I can't emphasize too strongly the fundamentals in Physics and Chemistry, Biochemistry and Physiology. They're absolutely necessary for any type of research. I think you get as good a grounding here as you can anywhere. Our graduates have gone all over the world, and made good.

Journal: What would you consider the most important difference between medical education in the 1920's and that of today?

Best: I think the volume of knowledge has increased so tremendously that I doubt that I could pass the examinations today!

Journal: Would you do things differently if you had a chance to do it all over again?

Best: I think I'd have taken more Physical Chemistry, although it wasn't difficult to get Physical Chemists to work with you.

Journal: What is your involvement now with the medical school?

Best: I lecture every year to the medical students, once or twice. For a long while, I had interviews with them if they had problems. I don't do so much of that now. Of course, I am invited to lots of other places. I was supposed to

go to Yugoslavia to get an honourary degree, but couldn't go because my wife was ill, and so they sent somebody here to bring us the parchment and so on. We were supposed to go to New Delhi, with all expenses paid, to the International Meeting, but we didn't go. It was in August, and it wouldn't have been too comfortable in New Delhi in August, I think. A lot of them got dysentry, so I'm glad we didn't go.

Journal: What else have you been doing since your retirement?

Best: My wife has been working at the family history, that of her family and mine, and we hope to publish a book some day.

Journal: Tell us about your family.

Best: We have two boys. One is a botanist, and an agricultural consultant. The other one is a historian. He's an expert on Maritime and Quebec history. He took his Ph.D at Laval, and now he's just been made President of Laurentian University in Sudbury. I don't think that's ever been announced in Toronto.

We have seven grandchildren. The oldest boy is 18 now, named Charles. He's interested in Medicine, and in Agriculture. He thinks he could do something where the two can be brought together. The oldest girl is interested in Medicine also, and she's very musical and artistic as well. It would be nice if one of them would enter Medicine.

Journal: What hobbies have you had?

Best: I have done some paintings; I have a number of them here throughout the house. I've also tried to ride horseback, wherever I get the chance.

Journal: Thank you, Dr. Best!

DEATH AND THE CORN LAWS

Frances Frankenburg 7T8

The passage of the Corn Laws in England together with some favourable weather patterns and a Dutch acid-base man led to a tremendous death rate in mid—18th century London.

The Corn Laws were a succession of laws regulating import and export of grain. Their purpose was to ensure high prices for producers while guaranteeing an adequate supply of grain for home consumption.[3]

The 1663 law for example imposed a duty on imported wheat and prohibited export when home prices were greater than 48 shillings a quarter. The Corn Bounty Acts of 1673 and 1689 rewarded farmers a bonus when prices of wheat, rye, barley, or malt were below a specified figure.

The effects of the laws were complicated by other changes in England; the commons were gradually being enclosed, leading to more efficient cultivation of public land, and agricultural technology was slowly improving. However the laws are generally credited with the increase in England's grain production. In the 16th century she was a grain importer; by the 17th century she was a grain exporter.

The years 1715-1750 had particularly good weather, and as a result the harvests in those years were excellent. One of the secondary industries that flourished because of the abundance of grain was the gin distilling industry. It employed English workers and used English raw materials, and it therefore was beamed upon by the English government.

Gin is an alcoholic drink made from grain mash and flavoured by the juniper berry oil. Juniper oil had long been known in folk medicine as a diuretic[2], but a professor of medicine, Franciscus de la Boe of Leyden (1614-1672), also known as Franciscus Sylvius, was the first to think of using it as an alcoholic

flavouring. Sylvius was an iatrochemist: he introduced the concepts of acidosis and alkalosis into clinical medicine, and therefore had a professional interest in diuretics. By mixing alcohol with juniper oil he concocted a drink with two diuretic agents and a pleasant flavour that rapidly became popular for its non-diuretic properties.*

The combination of the Corn Laws, the excellent weather, and Sylvius' genius as a diuretician led to a dramatic increase in gin production and consumption in England.

The English had always been boozers, but weak-drink-boozers, sticking with ale and beer. (In the Middle Ages the churches had afternoon ales instead of teas). In the country-side ale continued to be the drink, but in the 1700's the sophisticated Londoners were beginning to drink gin—strong and cheap —seriously.

By 1725 the city stocked over 6000 places selling gin. It was sold from "street-stall and barrows, from chandlers and tobacconists, from endless garrets and cellars."[7]

The gin parlours popped up with subtle signs: drunk for a penny, dead-drunk for two-pence, straw for three-pence.

Mortality and morality were elevated and depressed. In the first wild years the death rate climbed to a sobering one in twenty. (By comparison it was one in forty by 1821; in Canada today it is closer to one in one hundred and fifty.)

Why people died is not clear. It is unlikely that they died from the effects of chronic alcoholic diseases as the deaths were contemporaneous with the increase in drinking. Perhaps the other components of the juniper berry led to acute poisoning deaths. Gin was also heralded as a handy way of disposing of spoiled grains; this cannot have led always to the purest of drinks.

Mortality was boosted by the low levels to which the drinkers sank. Depravity and drunkards flowed freely and furiously with the gin. We see this

reflected nicely in the didactic paintings of William Hogarth. Beer Street (1751) shows jovial people drinking heartily from tankards of ale and radiating health and obesity; Gin Lane (1751) shows scrawny Londoners tossing down their gin as they toss away their miserable babies with sordid abandon.

The lawlessness and violence was annoying to the respectable Londoners. It was a danger to their own lives and property, and a constant aesthetic insult. Henry (Tom Jones) Fielding after two years as a London magistrate wrote in 1751: "Gin . . . is the principal sustenance (if it may be so called) of more than an hundred thousand people in this Metropolis. Many of these Wretches there are, who swallow Pints of this Poison within the Twenty Four Hours: The dreadful Effect of which I have the Misfortune every Day to see, and to smell too."[4]

More serious to the English perhaps than the human toll or even the smell and sight of the Wretches was the labour toll: "(gin) deprives them of time, money, health, and understanding (and) renders them incapable of hard labour (so that the businessmen) are deprived of great numbers of useful hands which would otherwise be employed to the advantage of the publick."[1]

The government was in the grip of the grain-growing-gin-distilling landowners, who themselves were undoubtedly lapping it up, but it was soon apparent to the most Korsakoffianly befuddled of gin-induced psychotics that England's wellbeing was diuresing down the gutters of London.

A number of attempts were made to curb the drinking. In 1736 for example Walpole's Gin Act imposed a 50 pound licence on gin retailers. Drunken riots ensued, the acts was ignored, and seven years later it was repealed.

The government perseverated. In 1751, the "Tippling Act" was passed, and it stayed passed. The act increased duties on imported gin, and, more importantly, forbade distillers, chandlers, grocers, and jail and workhouse keepers to sell spirits.

Harvests were also deteriorating at the time, and tea was beginning to attract the attention of the fickle English thirst centers; but it was the Act that was responsible for stopping the drinking. Gin consumption was 8½ million gallons in 1751; one year later it was less than 6 million gallons, and by 1800 it had dribbled down to less than 2 million gallons.[5] The Act was acclaimed as "a turning point in the social history of England and was so considered when this time was still within living memory."[6]

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Medical Career Choices at the University of Toronto: An Introductory Exploration

by

A. L. Ciavarella M.A. 7T8
P. N. Byrne Ph.D. DSME
J. W. Steiner M.D. Associate Dean

Dr. J. W. Steiner, The Division of Studies in Medical Education and the first author of this paper have been conducting studies into the career pathways and career choices of the University of Toronto Medical School Graduates. The survey work began in 1967 and will continue in the future. To date, there have been approximately 10,000 questionnaires gathered from about 2,000 medical graduates since 1965.

The members of each class of graduating medical doctors have received a questionnaire inquiring about their medical career plans, career intentions and possible factors that may have influenced their career paths. Each graduating class was subsequently followed on an annual basis for up to seven years. From this data base it has been possible to describe the various career choices and career pathways that have lead to the many possible careers in the medical field.

In collecting these data, three principles of confidentiality have been observed:

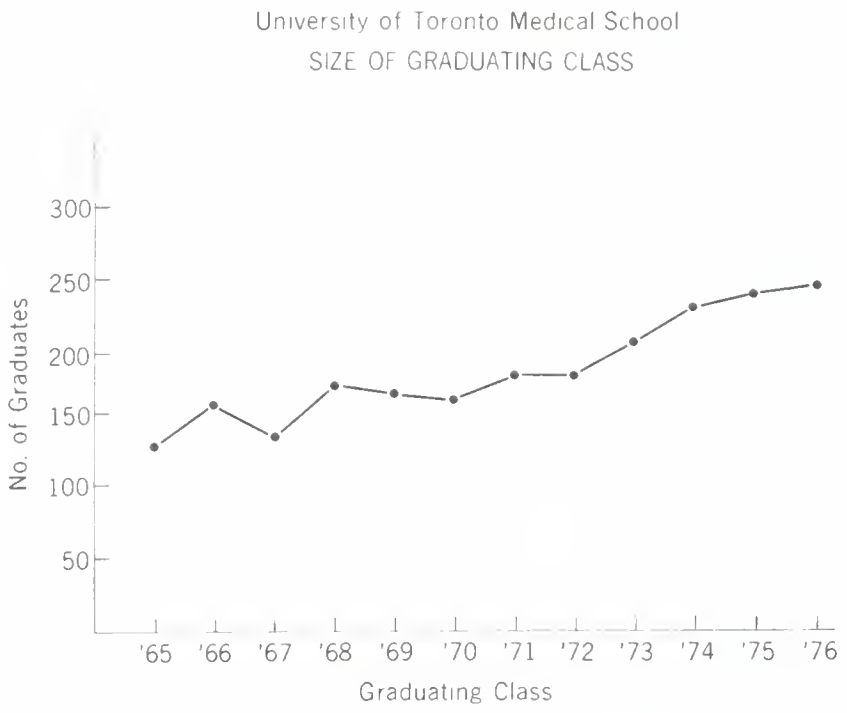
1) Information received for the study is strictly confidential
2) The identity of each respondent is held in strict confidence
3) Only information on general population and sub population career activities and pathways may be made available.

The response rate to this survey work has been most impressive. Over 90% of the graduates answer and return the questionnaire sent to them in their first year after graduation. This response rate has gradually diminished with each year following graduation, largely as a result of attrition and loss of contact with respondents. Overall the response rate has been well over 70%.

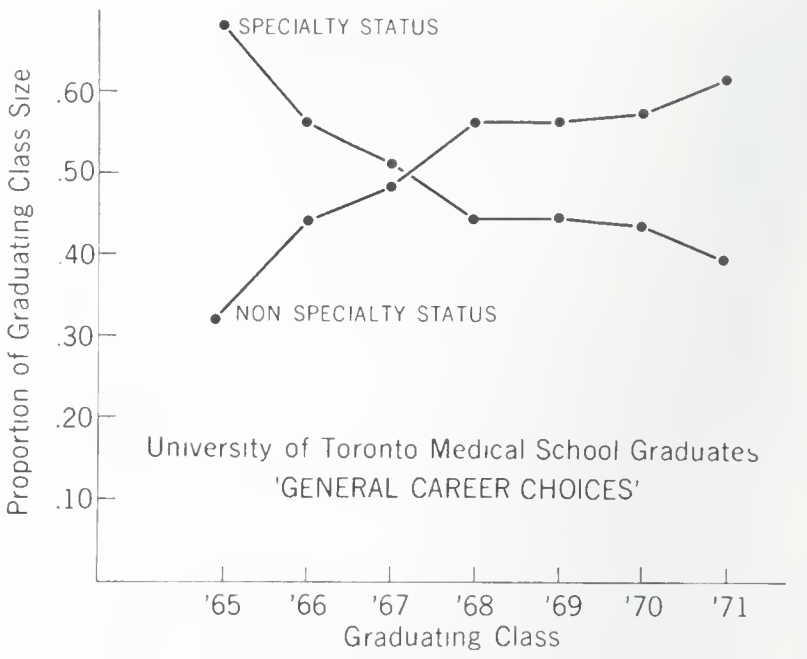
For the purposes of this paper, the term "career pathway" is intended to be synonymous with "career choice".

The summary data is now beginning to produce some interesting observations concerning the career choices and career paths of the graduating classes of the University of Toronto Medical School. It is hoped that this "History of Information" may be of some use not only to the medical planning bodies, but also to the career-conscious and often career-confused medical student.

At this point, only observations on career activities are presented. As yet, no overall conclusions have been derived from the observations.



The number of University of Toronto Medical School graduates in each of the classes from 1965 to 1976. (Information supplied by The Records Office, Faculty of Medicine, University of Toronto).



The ratio of specialty to non-specialty status career choices has completely reversed itself over the span of seven graduating classes from 1965 to 1971. In 1968 the non-specialty status became dominant and continued to do so through to 1971. There is some evidence that this trend has stabilized and will continue for a number of years.

Observations

(A) Size of Graduating Classes, 1965-1976

Since 1965, the number of people graduating from the University of Toronto Medical School has almost doubled, ranging from 126 in 1965 to 241 in 1976 (Fig. 1). The career pathways of these people have differed somewhat from class to class.

(B) Specialty vs. Non-Specialty Pathways, 1965-1971

Taking a very general perspective, it is of interest to inquire if any observable trends exist in career pathways. Indeed, this is the case.

Figure 2 considers the general career choice of the 1965 to 1971 classes with respect to a specialty (e.g. FRCP) or a non-specialty status (e.g. G.P. or Family Medicine). From this data it is evident that the proportion of graduates with a career path leading to a permanent non-specialty status is increasing, whereas the proportion of graduates with a career path leading to a permanent specialty status is decreasing.

That part of the class with a career path indicative of a non-specialty status increased from 32% in the Class of 1965 to 61% in the Class of 1971. Similarly, that part of the class with a career path indicative of a specialty status decreased from 68% in the Class of 1965 to 39% in the Class of 1971.

Over the span of seven graduating classes from 1965 to 1971 the ratio of specialty to non-specialty status career pathways has completely reversed itself, with the non-specialty status pathway becoming dominant in 1971. There is some evidence that this trend has somewhat stabilized and will continue on with the 1972 to 1976 classes. As more information is gathered on these classes, it will be possible to make a somewhat more definitive observation in this regard.

The proportions given in Figure 2 stop with the class of 1971, because of the criteria used to determine the most likely career pathway that will become permanent for each candidate. This determination is based on academic and professional performance over a six year span and thus necessitates the termination of the trends displayed in Figure 2 with the Class of 1971. It should be pointed out that these "observed career pathways" are those pathways considered to be most likely, based on the information available, but are in no way binding or absolute.

(C) Specialty Status Career Pathways, 1965-1971

The group of respondents with a specialty status career pathway is a rather diverse one. It is possible to make some very interesting observations about these respondents by adopting a very simple approach.

This group of respondents is divided according to the general disciplines in the medical field. These general disciplines have been taken to be surgery, medicine, laboratory and academic research.

The surgical discipline includes surgery with all of its subspecialties, (e.g. neuro-surgery), along with the surgical related field of ophthalmology, otolaryngology, obstetrics, gynecology and all of their respective sub-specialties.

The medical discipline has been taken to include medicine with all of its sub-specialties (e.g. cardiology), along with the medical related fields of anesthesia, radiology, nuclear medicine, paediatrics, psychiatry and all of their respective sub-specialties.

The laboratory discipline includes pathology with all of its sub-specialties along with the laboratory related fields of clinical biochemistry and medical microbiology.

The academic discipline has been taken to include any medical doctor whose career pathway has lead to a position of full time academic research at the Ph.D. level.

Figure 3 illustrates the proportion of graduates in each of the classes from 1965 to 1971 whose career pathway has lead to each of the respective disciplines.

The sub-population of academic researchers shows a precipitous drop from about 10% in 1965 to practically 0% in 1966, continuing through to 1971. The laboratory sub-population also shows a meagre display of popularity. Whether these observations indicate a possible shortage of personnel in these two disciplines is not at issue as any possible local influx of manpower immigration from other parts of Canada and immigration from foreign medical schools may fill gaps in a free marketplace situation. However, evidence seems to indicate that the University of Toronto setting is not renewing its own human resources in the laboratory and academic research disciplines.

The medical and surgical disciplines attract the majority of the University of

Toronto Medical School graduates in the specialty field. Over the span of seven classes from 1965 to 1971, the medical discipline shows an overall greater popularity than the surgical discipline. Each group shows an interesting waxing and waning pattern, reflecting a mirror image of the other. Although the medical discipline shows a somewhat greater popularity trend than the surgical discipline, it is not increasing in its own right; whereas the surgical trend shows a definite decrease over the span of 7 graduating classes.

(D) Career Information and Career Counselling

Medical students of the past have all made some type of career definitive decision at one time or other. One question raised by the study concerns the availability of information on career possibilities and also adequate access to career counselling. The averaged results from a number of populations over a seven year span are depicted in figure 4.

The respondents were asked the two following questions:

a) Was sufficient information available during medical school on the career possibilities in medicine?
b) Did you feel that you had adequate access to counselling on career choice during medical school?

The majority of respondents gave a negative response to each of the above questions. It is of interest to note that the proportion of "no" respondents increased with the number of years after graduation, stabilizing after the third year. The observation is made that a significant majority of medical doctors believe that there was a lack of career counselling and also a lack of information on career possibilities while in medical school.

Tentative Conclusions:

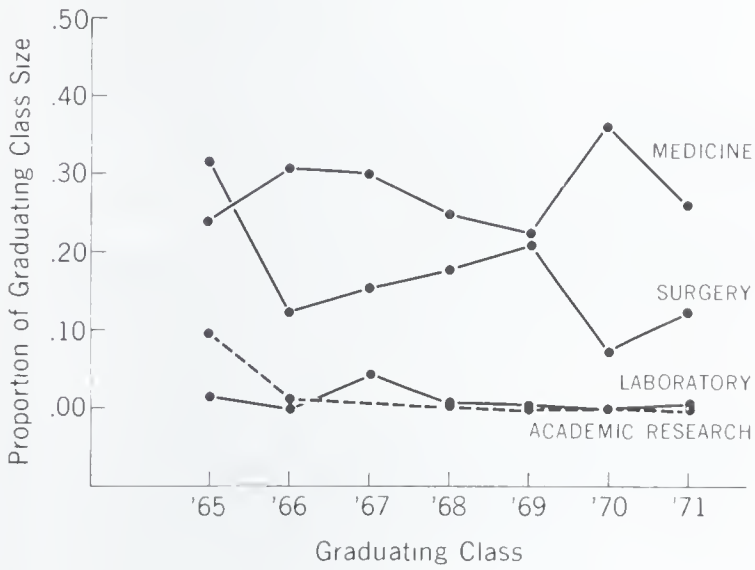
The career data offered in this paper represents the tip of an iceberg, by describing some basic information concerning career pathways of graduates 1965-1971. No attempt has been made to analyse the factors that have affected choices and pathways; nor has any attempt been made to explain the observed changes in career patterns over the time span 1965-1971. A number of analyses are presently being conducted to establish a rational means of explaining the observed data. In due course these analyses will be published.

From the work completed on career choice surveys to date, two major implications are necessarily raised. The first of these implications relates to effects of career choice data on planning, both in terms of curriculum and of manpower. It is clearly of interest to the medical faculty decision makers to know the trends of career pathways and choices of graduates and to have this information as a basis for deciding on residency program needs. General questions remain to be answered before such information can be put to use. For example, pathways and choices dates subsequent to 1971 graduates are required. Also, the probability factors affecting career choices require documentation and the reliability of the information must be substantiated.

The second implication of the data presented has to do with the persons, students and residents, who are in the process of deciding upon pathways and careers. Again many questions of further information need to be raised and answered, not the least of which is the impact of government policy on choices. Moreover, data on appropriateness of pathway and career decisions of previous graduates is viewed as useful information to students and doctors in making their decisions. A counselling career service for students, however immediately desirable, needs a bank of accessible information containing the information described above and, in addition, containing representative detailed descriptions of the activities of different types of doctors, not only in terms of specialties, but also in terms of rural vs urban practice, teaching hospital vs non-teaching hospital and so forth.

The data shown in this paper is viewed as the beginning of the process of conveying information to students in the service of enabling them to make appropriate career choices.

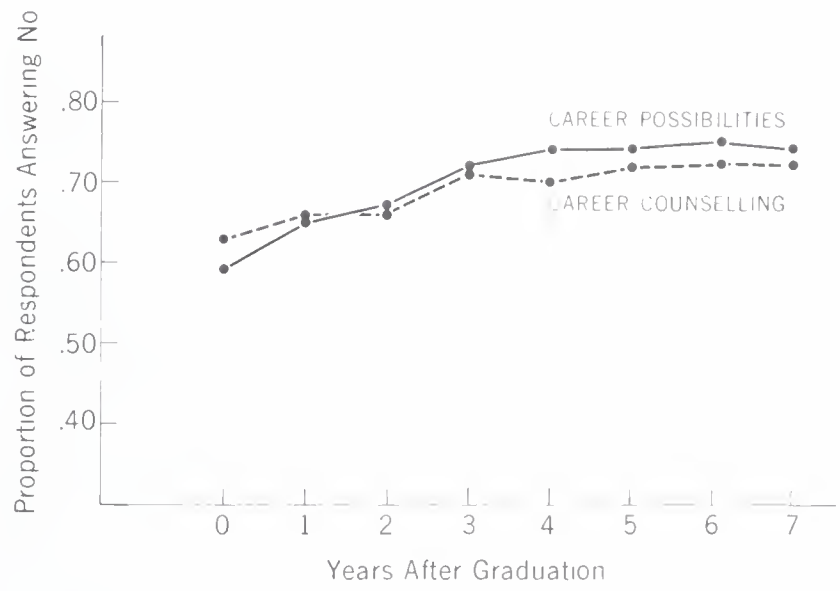
University of Toronto Medical School Graduates
SPECIALTY STATUS CAREER CHOICES ; 'DISCIPLINES'



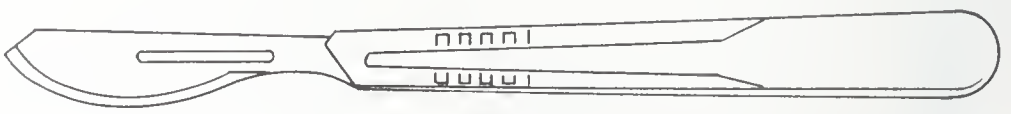
Over the measured span of graduate classes, the medical and surgical disciplines have attracted the larger majority of the respondents. The laboratory and the academic research disciplines have attracted a very small minority of the respondents, if any at all.

The medical discipline shows a non-increasing or decreasing trend, whereas the surgical discipline indicates a trend that is decreasing in popularity.

University of Toronto Medical School Graduates
CAREER INFORMATION AND CAREER COUNSELLING



The majority of respondents felt that while in medical school, information on medical career possibilities and counselling on career choice was not adequate or sufficient.



Medical School Admissions Criteria: Are Marks the Measure of the Good Physician?

Pro

I feel that the best indication presently available of how well a person applying to medicine will later perform as a practising physician is his/her previous academic record. This is not to say that other factors such as interviews or work experience should not be taken into account, but rather that *marks* are the single most important factor and, as such, should be heavily weighted in any medical school admission policy.

The view I have taken may seem contrary to the current trend of thought that physicians need to be more human and empathetic, and less rigid and impersonal. (Communication's the thing, man!) Many people feel that human compassion is a more important quality in medical school applicants than is scientific knowledge and basic intelligence. To these people, I say that human compassion is an important quality in physicians, perhaps equal to scientific knowledge, if they could be equated. However, no admission procedure, existing or proposed, is able to evaluate something so ethereal as human compassion. Also, the scientific knowledge is a necessary prerequisite in order to understand most of the content of medical school, whereas nothing in the present curriculum requires a prerequisite of human compassion. Therefore the human element can be acquired during medical school, and does not require admission procedures designed to select those people who are the best at interpersonal relationships.

Let us examine what type of person is selected by an admission policy based mainly on academic records. A person who obtains high marks must either be fairly intelligent or be hard working and determined, and most likely is a combination of the two. Is this the type of person that it is desirable to have in medicine? Obviously yes! Medicine, I'm sure you will agree, requires more dedication than the average Canadian occupation. Also, it requires a reasonable degree of intelligence, the more the better. (Of course, a person may have achieved high marks by devious methods—cheating, bribery, breaking into the computer memory bank holding the marks—showing intelligence of a different kind, but I don't think this is very widespread).

Now to deal with all those objections that are springing to your lips, about the meaninglessness of marks and how they select for the one-sided book worm who spends 16 hours a day studying. It is true that the marks are not uniform, that some universities may be slightly easier than others, and that certain ("avian") courses may be easier than others. This is where the one true fault with using marks as the sole admission criterion lies, and why other ancillary factors about a person should be taken into consideration. As for the argument that a person who has achieved high marks must be one-sided and poorly "cultured", this can quickly be dismissed by a look at the multitude of different interests and hobbies medical students have.

What alternatives do opponents of a mark-oriented admission policy suggest? There is the personal and group inter-

Con

What follows may be unpalatable to many of you since all of us who are U. of T. medical students have been selected primarily because of our 'academic excellence' (Faculty of Medicine Calendar) as measured by our transcripts. I have nothing against 'academic excellence'; it's a fine admirable concept, and something well worth achieving! My quarrel is with the use of a *university transcript* as the *major* criterion for determining who is admitted to medical school. I don't intend to argue the point that such a system unfairly excludes many people who would become competent doctors. This is, of course, true, but virtually any system designed to select just a few from the many qualified applicants will necessarily exclude sizable numbers of people who would have been admitted under different criteria. Rather, my argument is that the emphasis placed on the accumulation of high grades as the major prerequisite for admission is actually counterproductive in that it encourages and rewards behaviour which ill serves the practice of medicine. Let me illustrate my point with a scenario. I apologize in advance to those of you to whom my generalizations do not apply.

You're 18, in first year university and you want to become a doctor. The task immediately ahead of you is pretty clear—you must get 'A's in virtually all your courses over the next two or three years, and the time to begin is right now.

If you're wise to the game, you begin by taking the easiest, least demanding courses you can get away with. Why sweat over Math 199 when Math 100 counts equally as a prerequisite? This isn't meant to imply that you are lazy or unmotivated; you're actually going to work your butt off, but in the algebra you understand so well . . . course grade is proportional to the effort expended and to the reciprocal of the difficulty. Why jeopardize your chances for an 'A' by taking a challenging course? As for your 'extra' courses, the ones you take to make up five credits, God forbid that you should attempt anything outside your existing areas of competence, unless it's a 'bird' course where the professor gives 'A's to all the students in the misguided view that this will 'undermine' the system. Actually, the best courses to take are those for which you have already done some of the work—you may even have a suitable essay available—since this way you can get your high grade and still have time left over to patch up any weak spots. With regard to your level of achievement, you're a firm believer of the relativity theory—it matters little how much (or little) you know but rather how much *more* you know than the people sitting on either side of you since they're likely to be pre-meds as well and you can't all get in. This is the pursuit of 'academic excellence'.

Then there's your non-academic development. "What's that?" you say. You know. . . . personal growth, new friends, new lovers, expansion of your high school-defined horizons, "Velut arbor, aevo" as the saying goes. "Well," you say, "All that stuff's a bit risky. My God, what if I had an emotional crisis just before an exam? I've even heard of people actually dropping out because of this 'expanded horizons' nonsense,

Pro *(Continued*

view approach at McMaster, where marks are of little concern. The type of person favoured under this system is the good actor or the person who is quickly at ease when talking with strangers. As I stated above, the interpersonal relationship component can be acquired during medical school, and is not the most important quality when seeking the raw material for medical education, while the selection of good actors is probably detrimental to the selection of good physicians. There is the possibility of placing more importance on personal references but the vast majority of people dislike this proposal since it simply becomes a matter of knowing people in the right places. Finally there is the lottery system for all applicants who are reasonably qualified (i.e. over 70 average in "undergraduate" courses). This reduces admissions to a circus-like policy, and is saying, in effect, that we have no idea what factors indicate that one person will be a better physician than another.

I believe that marks do give a good indication of how well a person will do in medical school and what quality of physician he will be after graduation. Other proposed admission policies are either negative (interviews) or neutral (lotteries) and provide no reasonable basis for accepting one person and rejecting another. Marks, although by no means perfect, are the best criteria we have at present to determine admission to medical school.

Wayne Gregory 7T9

Con *(Continued*

and where are they now? They sure as hell aren't in medical school." Alas, you're probably right. Any false or faltering steps you take could show up on your transcript and that's a monkey you'll never get off your back. In a recent edition of the **CMAJ**, medical students were described as exhibiting predominantly "repression of growth and creativity, isolation, an undue stress on productivity and achievement, and repression of aggressive affect and tender affect. Ours is a relatively unfeeling and interpersonally distant group with little creative spark." Is anyone really surprised?

What is the prize that draws so many bright, young, vigorous people to pass what should be the adventure-filled last years of their adolescence engaged in anxiety-ridden, self-denying study? Perhaps this is an exceptional group of teenagers mature enough to know themselves very well—their aspirations, abilities, limitations—and who also know medicine well enough to be sure that it will provide sufficient spiritual as well as material sustenance. Then again, this could be an unexceptional group who, like their peers, are just getting to know themselves but who have become beguiled by the image of the physician and have decided that there's no need to look further. Both explanations can account for the flock of dedicated pre-meds.

The 'academic excellence' system of selecting medical students encourages a cynical, narrow-minded, fundamentally anti-intellectual attitude towards learning. By punishing failure so severely, it channels students into 'safe' endeavors and 'safe', i.e., timid, ways of coping with personal struggles.

Probably all selection systems have flaws and biases, but it is hard to imagine a system which, to a greater extent, fosters attitudes and behavior so antithetical to the practice of good medicine.

David Arnold 7T9

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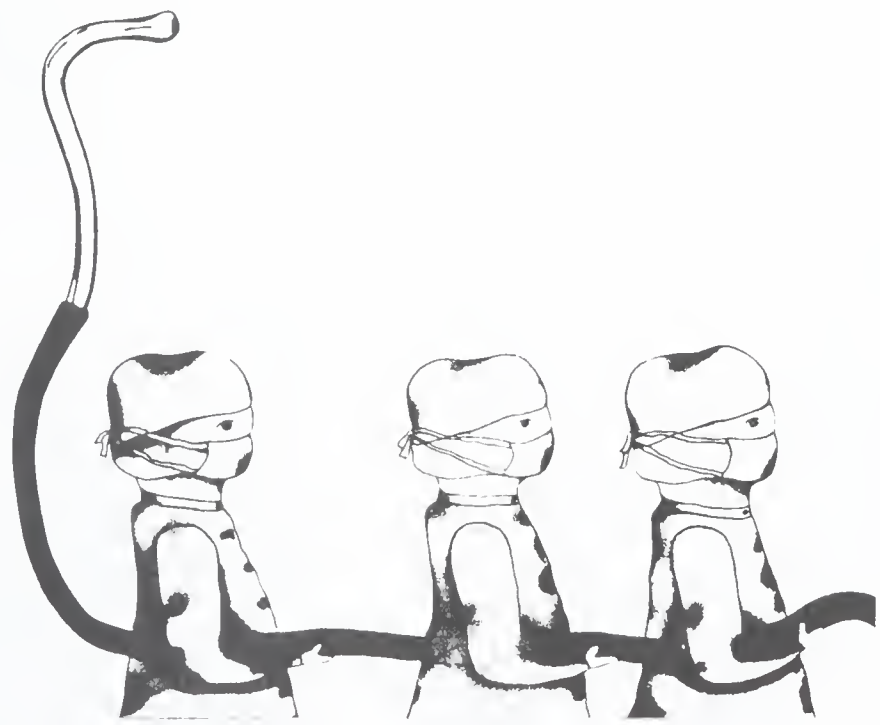

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Sexuality and Medicine: Who's Responsible?

Randy Gangbar 7T9
Sarah Lazier 7T9
Bob Sauls 7T9
June Kingston 7T9

The January, 1977, issue of this journal carried an article written by Susan Ross, 7T9, entitled "Sex and the Medico—Not Just More B.S." which discussed the teaching of human sexuality within the medical curriculum at the University of Toronto. Motivated by this article, we felt the need to expand on some of the issues involved and to put forth some of our personal feelings and ideas concerning the learning and teaching of human sexuality and the respective roles of student and teacher in this process.

It has been said that we are feeling the effects of a "sexual revolution" which for us as medical students takes on an added significance in that more and more the physician is being called upon to wade in the muddy waters of the aftermath of that revolution. Increasingly, the physician is finding him/herself confronted with the dissatisfactions, confusions and casualties resulting from that revolution, as well as the problems that existed prior to the revolution and which have just now found channels for expression. And, in general, the physician is being strongly urged to begin to consider the sexuality of his or her patient as an important element in the overall picture of the patient. These demands, quite understandably, have been passed along to medical educators with a word of admonition that they begin turning out physicians who not only have a knowledge of the basic biological facts of sexuality but who are also capable of dealing effectively with the sexually-related problems of their patients. Medical schools have, to the satisfaction of some and the dissatisfaction of others, responded with a variety of presentations of human sexuality. Here at the University of Toronto, under the auspices of the Behavioral Science Department, medical students have been offered a course as well as an elective dealing with the subject. The question, however, arises as to whether medical educators here have adequately satisfied the demand. The same question of responsibility does not arise quite so often for ourselves, the students.

To get an idea of the scope of the problem, maybe we should take a look at the sexual revolution itself. It might be said that, growing up during this revolution, we as medical students represent a new breed of physicians who are equipped to deal openly and effectively with the sexuality of our patients. But, is this actually the case? Turning to the rhetoric which we've listened to, our impression is that the sexual revolution has been concerned with freeing us from cultural and personal anxieties, inhibitions and outright fears in order that we might openly and unashamedly express our very natural sexuality. No longer need we repress our sexual feelings and desires because of moralistic and sexist attitudes; no longer need we deny a large part of our emotional make-up. Have we accomplished all this, more so than generations in the past? It's obvious that we've liberated our desires, or at least, we've brought them out where everyone can see. We now live with our lovers; we have brief sexual relationships in pairs or groups; and we openly proclaim our personal sexual orientations. It would seem that the doors have opened, that we can, at last, be our natural sexual selves. But, we really must look deeper than this, for freedom rarely comes without an attendant responsibility. We must ask ourselves whether we've come to some kind of awareness of anxieties and frustrations, of our attitudes and biases concerning sexuality, regardless of whether we wish to change them or not. In our opinion, we haven't carried this part of the revolution very far; it seems that we're still quite frightened by it all.

Making the assumption, then, that we have not come as far as we would like to believe, how will we complete the process? For us as medical students this becomes a crucial issue, for, inevitably, we will deal with our patients' problems in much the same way that we've dealt with our own. Where, then, shall we place the responsibility? It is our feeling that the responsibility is a shared one with a part to be played by our teachers and a part by ourselves. The responsibility of our teachers would appear to be concerned with providing us with the tools we will need to confront the sexual problems of our patients. In consideration of this, we might ask that our teachers provide us with 1) basic information about the biology and psychology of human sexuality, 2) an exposure to the types of problems we might be faced with as physicians, 3) access to resources, bibliographies, etc. to which we can turn both during our later years of medical school and after we've left medical school. But tools without the ability to use them are quite useless. It's here that we must assume our part of the responsibility. Of primary importance, at least for the present, is that we carefully examine our own attitudes and feelings concerning sexuality—what does our personal sexuality consist of; where do our fears lie; how do we feel about sexualities different than our own? Our task, here, may be much more difficult than that of our teachers, as we will have to confront those feelings which may evolve a sizeable amount of tension, and those may be the very feelings that most need to be examined. We feel that this is a basic requirement; this is the first step. Beyond this, our responsibility demands that we make use of the resources that have been put at our disposal. The field of human sexuality is extremely broad, and any course can only serve as an introduction. We must take the respon-

sibility of further educating ourselves.

So, how do we fare? Have we assumed our part of the responsibility? It's our opinion that our teachers have picked up their end quite effectively. A glance at the list of topics covered within the course we were offered will reveal that few stones were left unturned; we were presented with an ample amount of information, exposure to problem areas, and resources. In addition, we were provided with the opportunity to fulfill our end of the responsibility within the context of seminars aimed at allowing us to examine our own feelings and attitudes. Inevitably, there are areas which could be improved upon, but for the most part, our teachers have performed quite well and are definitely headed in the right direction. But what of ourselves; have we assumed our part of the responsibility? We haven't done quite as well. For the most part, we have sat back waiting for a truly relevant presentation of human sexuality, when the only truly relevant presentation is the one we make to ourselves. The only real failures of the course and seminars were our failures due to an unwillingness to respond with a careful look at ourselves. The quality of any presentation on human sexuality will only be as great as the effort we, the students, put into it. Teachers can provide us with information and direction; the actual integration and learning is something only we can initiate.

ELECTIVE CIRCUS

The Lighter Side of Student Research (or "This Time for Sure!")[1]

by Jay Wortsman 7T9

I study and I hear "Bolero". That's so, and not just in my resting imagination either, oh no! I would hear it while I tried to commit the brachial plexus to memory. Nothing too loud, mind you, not then anyway. Something of a soft, slow, seducing sound. A passing procession . . . daahhhhh . . . daa . . . da da . . . da da . . . da da . . . daahhhdaahh . . . quietly droning on and on . . . daahh daahh . . . duh . . . duh duh . . . it's nothing. A catchy tune, just something that's seized my mind for awhile.

But it came again . . . in brain, bundle branches, bulbar tracts, beri-beri . . . BARR BODY . . . DUH DUH DUHHHH DA DAAHHH . . . and it stayed longer and was louder . . . DAHH DUHH DUHH DUHH DU DUHHH . . . and it wouldn't let me sleep or . . . DAH DAH DAH DAH DUHH BUM BUM DAAHHH!! It went on and on until I found I could memorize no more . . . DA BA BA DUHHHH . . . without provoking its wrath DAH DUH DAHHH . . . I sought escape in more sleep but it pursued me while I conducted billions of bacteria all humming bass DAAHHH DA DA DA DUHHHHH!!! . . . Other diversions, I tried exercise, exhaustion, comic books, T.V., but on and on it came at accelerated tempo to the rhythm of watchbeats, rain drops, dogs walking on linoleum, obese tap dancers . . . DAHHH DAHH DAHH DUM DA DA DUHHHHH . . . I NEEDED RELIEF . . . I NEEDED AN ELECTIVE!

That was it. It's gone. So simple, Feh!! An elective. I would do something in my elective time that would re-unite me with my forsaken science, with irreproachable reason, with my beloved problem-solving algorithm . . . and no more memory work, not for this. But what would I do?

Fortunately, I knew of a laboratory offering hard work in exchange for free labour, and so I jumped at the opportunity, competing all the while with postdoctorates also looking for work. It was to be in Endocrinology . . . the Science of Medicine . . . OH JOY! All prayers are answered, even for we atheists, it's hard to miss that smile from above!

My mission, I was to learn, was to assist in the creation and implementation of a diagnostic test that would be applied to neonates with ambiguous genitalia having the syndrome of male pseudohermaphroditism. My constraints were that I use *in vitro* techniques and, with a radioactive marker, follow this marker through a cell's metabolism to test for its appearance or non-appearance. In other words, to test for the cell's ability to utilize this labelled substance. Now there's SCIENCE! But what was male pseudohermaphroditism? Off to the literature. . . .

Male pseudohermaphroditism is a catch-all term for any abnormal alteration in the physiological development of the karyotypic XY embryo. It can occur due to either of two main disturbances of metabolism of androgenic hormones: 1) A defect in the enzymatic path in the formation of testosterone (T) from cholesterol but occuring in a site other than in the target organ. 2) A disorder in end (target) organ function.

The first case, those with an enzyme deficiency or defect, was straightforward enough. There are eight known enzymatic reactions in the conversion pathway of cholesterol to T and a defect has been described for each step.[2] These defects may be only slight and so cause minimal metabolic and physiologic upset (e.g., and isozyme may form with reduced activity), or it may be so severe as to be deficient in the enzyme. Therefore, children born with this syndrome may show only mild forms, with only slight feminization, or run the course to appear phenotypically female and not usually be suspected until puberty when they present with amenorrhea. With this latter type of patient, they may present with inguinal hernia with testes in the inguinal canal or labia majora. In any case, if one biopsies for testicular tissue and can show with *in vitro* studies that the patient is responsive to the end product T, then an androgen hormonal therapy schedule may be of immense benefit to the patient depending on the severity of his condition, and, if it was caught pre-pubertal or not. One could show experimentally where the enzymatic defect lay by incubating the tissue samples with cholesterol and collecting metabolites for analysis. Replacement therapy could then allow the patients to overcome their metabolic deficiency, depending on the severity of the phenotypic development.

The second case, however, was a little more complicated and serious. In

this form of the syndrome there are three subpopulations: the complete form of testicular feminization (TF) and the incomplete forms, with Types 1 and 2.

In the complete form of TF the testes differentiate normally and plasma levels of T are in the normal or even high male range. Despite this, the child will have female external genitalia, with a short vagina ending blindly, but will not have a uterus or fallopian tubes. The syndrome is postulated to exist because of a defective or lacking cytosol receptor protein that transports T or dihydrotestosterone (DT) from the plasma membrane to the nucleus where these hormones exert their influence on DNA[6,2,3] This form of the syndrome is the one I experimented with. One would culture fibroblast cells from the perineum, which cells have been shown to be the most responsive anatomic site to T[5] in males and females[6], with labelled T and/or DT. The tissue culture preparation would be fractionated and the cytosol receptor complex isolated, if it were present. If it were not present, then female hormonal therapy at puberty would likely be the best treatment for this patient who is unresponsive to androgens. (Un)fortunately someone had already performed the experiment, but it would be a simple matter to reproduce their results in Toronto[7].

The incomplete form of TF, Type 1, has been described under the various names of Reifenstein, Lubs, Gilbert-Dreyfus, and Rosewater Syndromes, depending on the severity of the syndrome's manifestation.[8] Patients, as in the enzymatic defect form of male pseudohermaphroditism, can present with minimal virilization defects or be as extreme as the complete TF-like syndrome. The metabolic defect in this case, however, is not known, and so would not be experimentally testable.

Type 2 incomplete TF (also called pseudo vaginal perineoscrotal hypospadias) presents with severe hypospadias and underdevelopment of the vagina. They are usually classified as phenotypic females.[9] It resembles Type 1 except that it is not X-linked inherited, as Type 1 and the complete forms of TF are, and gynecomastia does not develop at puberty, as it may in Type 1. The defect here is thought to be due to a deficiency in the cytoplasmic enzyme 5α reductase, which converts T derived from plasma into DT in the target tissue cells. This form of the syndrome would then be easily investigated experimentally with labelled T and a subsequent search for the label in the DT metabolite.

The experiment itself was simple. All I had to do was grow some fibroblastic tissue in vitro and culture it with labelled T for 10 or 15 minutes, wash out the excess, take the cells and spin them down in a centrifuge, then take this cell pellet, disrupt the cell membrane and play out the cytoplasmic solution on a Sephadex column. Not quite all, but enough for now.

Well, novice that I was, I was prepared to tackle anything. I ordered all my supplies and made up all my buffers. Arrangements were made for me to fetch normal foreskin tissue from two newborns at the ungodly hours of the morning. All went well, everyone cooperating to their fullest, even the little nippers who contributed most to my experiment. I was ready now. ONWARD!

First I needed a control, like any other good experiment. I reasoned that if the experiment was to measure the supposed lack of a cytosol receptor it might be good to find a substance that competes with DT or T to block their respective bindings to the receptor protein. I could have used unlabelled DT to compete with labelled T and DT, but that was too drab. I wanted some real planning! By this time, word had spread to the other fellow in the lab and I also asked him if such a compound existed to act in my control for normal skin. He had just the thing. Apparently an anti-androgenic compound had been sought, synthesized, and even used on volunteer prisoners with unusually pushy behavior. It was supposed to work by just such a method as cytosol receptor blocking. There was even some of this drug in Toronto, at the Clarke Institute. OH JOY! . . . that smile from above again!

Off I went to the Clarke to gather a tiny bit of this heavensent drug. The researcher working with the compound (cypoterone acetate) took out a plastic pouch and teaspooned a small quantity in a vial for me. He said not to worry about its effects on me, while it was in powder form anyway. He must have known, but still, I couldn't get over the beards on his hands. Well, anyway . . . ONWARD!

Next, I had to work out the manner of cell disruption. The scientific catalogue had some beautifully efficient, professionally engineered machines, some capable of reducing a whole mouse to sub-cellular fractions in less than 30 seconds. Impressive. A little too enthusiastic for my needs, however. Instead I chose a slightly more subtle method that employed ultra-sonic vibration. It would shake the little plasma membranes to tiny bits, leaving intact cytoplasmic contents. It had one drawback, mind you. It also shook the old tympanic membrane to bits, necessitating the insertion of tiny rubber test tube stoppers in my ears. An inconvenience. Onwards!

What was left? Just do the experiment, write it up, and feel brilliant! Feh!! Research . . . onwards!!

Trial 1: We won't expect spectacular results here. It's our first time . . . just starting. I ran the experiment exactly as it was worded on my handprinted protocol sheet. Cell selection, incubation, centrifugation, ultrasonification, with accessory ear plugs, of course, and re-centrifugation. All went well, as anticipated . . . that is, until I had to fraction the sonicate on the Sephadex column.

I hadn't figured collecting 20 drops a vial, 20 vials a run, four runs an experiment, would take too long. Maybe an hour or two, and I could read while doing this. So I sat there counting the drops as they fell into my scintillation vials. One, two, three, four, four . . . wait, I had four, six, seven, nine, ten, twenty . . . looks a little small here. Evaporation.

Next. One . . . two . . . one . . . oh, ahh two, no, ahh three, four, five. 20X20X4 = 1600 drops. Eight years of elementary school, five years secondary, three post-secondary, and I'm counting 1600 drops? Seems I recall a water torture like this. They should get an idiot to do this . . . err?

Three hours later I added the scintillation cocktail. If I didn't feel like a myrmidon by now, this little activity was no help. I aliquoted out 10 cc/vial for 80 vials. I also developed toluene-induced hepatitis. Onwards!

Into the scintillation counter I place my cherished work, my *magnum opus*, my life's creation. On go the switches, the timers, the radiation window settings. I am about to see the fruits of my dedication. Pushing the start button and . . . fanfare, Gregorian chants, and Nobel Prize speech . . . the machine blinks KNDWIN6LT, whirrs its approval and obediency and tenderly cradles the first vial into its electronically precise, quantitatively correct, photosensitive crystals. It's purring anticipation. Quiet . . . it's about to relay the information via its satellite teletype. PLIKA DADADA PLIKA it says. I read, "1. 2.00 20.00 20.00 1.00". I translate, "Vial I timed for 2.00 minutes. 20 photoemissions registered in channel A, 20 photoemissions registered in channel B. The ratio of A/B is 1.00". It has spoken! Onward!! Vial number 2. WHIRR BUZZ CLICKEN HUMM. PLIKA DADADA PLIKA 2. 2.00 19.00 20.00 0.950. AHA! A significant change in channel A! Obviously the more accurate one! IT'S WORKING! PLIKA

DADADADA PLIKA **3**. 20.00 20.00 1.00. What's this? Maybe . . . no. It's working! **4, 5, 6, 7, 20** . . . 20.000 20.00 1.00. Vials **21-40**, **41-60**, **61-80**, 2.00 20.002 **00** 20.00 2.00 1.00 2.00.

WHURR BUZZ WHIR PLIKA DADADA PLIKA Stand-by . . . Stand-by . . . Stand-by. Ready for more, Boss . . . this is fun . . . WHIRR BUZZ CLICKEN. I killed the machine. I chopped its plug off.

Trial 1 (TN1) gave me small success. I was now an expert on man-machine interaction and psychology and I was able to plot a perfect background curve. So there! Onwards! **TN2**: Seems I missed a small point about taking the Sephadex fraction in the cold since the cytosol receptor complex was extremely heat labile. Oh well, that's alright. I'm expendable. Ever sit in a cold room at 4°C for the better part of an hour? (I had decided I need only do one run to demonstrate success), changing vials after one ml. of buffer solution had come off the Sephadex column.

I tried using the department's fractionator/collector. A simple enough machine that is fully designed to replace me. It would even count out 20 drops per vial, change tubes, and do it again, and ENJOY it. All while I slept or ate or cried . . . unfortunately the owners decided it was contaminated with radioactive iodine someone accidentally spilled on it after I asked to use it. That's alright. I wanted to dedicate my life to Science anyways.

WHIRR BUZZ CLICKEN PLIKA DADADA PLIKA **1**. 2.00 20.00 20.00 1.00. pause

NOW AIN'T THAT A KICK IN THE HEAD? "The best laid plans of mice and men . . . "

TN4: "This time for sure".

I retraced my procedural steps. Strictly adhering to the experimental protocol, I ensured that all quantities of ingredients were accurately weighed, all cell cultures properly maintained, all my financial matters attended to. It would work this time. The procedure went like a charm. I had by this time encountered and anticipated every conceivable foul-up and every mishap. I even brought provisions in the event I had to stay a little longer. One can never have enough pretzels.

I was ready now to face **THE MACHINE**.

TN6: "This time for sure, with a control, this time for sure". I'll use unlabelled normal DT instead of fancy-schmanky cyproterone acetate.

TEST: 20 25 40 35 20 110 70 40 20

CONTROL: 20 20 20 20 20 20 20 20 20

A little too much DT or something

TN9: I have decided that my control DT concentration was a little off, so I changed it slightly from 10^{-7} molar to about 1 molar. The boss said to watch out that the cells don't attack me. I could break the joker's neck.

TEST: 20 25 40 25 20 25 110 70 40 20

CONTROL: 20 25 20 20 20 25 110 70 40 20

It works. . . . sort of . . . it's just a little backwards, a little error, that's all DA DA DA DUH DUH DAH DUHHHHH. . . .

Well, I'm still working on it . . . it will come, you'll see. Don't take these results too seriously.

I wish to express my sincere appreciation and gratitude to Dr. J. Bain at the Mount Sinai Hospital for his time, guidance, and sense of humour.

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The remaining references are available from the editors on request.

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